The New England
Journal of Medicine

VOLUME 209 NOVEMBER 23, 1933 NUMBER 21

NEW ENGLAND SURGICAL SOCIETY

ABDOMINAL SYMPTOMS WITH OR WITHOUT ABDOMINAL LESIONS IN DIABETIC ACIDOSIS*

BY LELAND S. MC KITTRICK, M.D.†

INTRODUCTION. On September 25, 1927 at one o'clock in the morning, a sixteen year old diabetic girl entered the Emergency Ward at the Massachusetts General Hospital. She had awakened the preceding morning with signs of a cold, had no appetite, and did not eat as usual. At 7 P.M. there was nausea and vomiting, at 9 P.M. there was sudden, severe, non-radiating pain in the epigastrium, not cramp-like, for relief of which she was brought to the hospital. She was slightly drowsy and had an acetone breath. Examination was otherwise entirely negative except for exquisite tenderness across the upper part of the abdomen. There is no note in the record of the absence or presence of spasm, or of any point of maximum tenderness. She had a white count of 31,500. Urine showed a red precipitate with Benedict's solution, and diacetic acid. Temperature was 98.8 by rectum; pulse 100; respirations 30. She was seen by the emergency ward surgeon who made a diagnosis of acute pancreatitis and advised immediate operation. At 4 A.M. laparotomy was performed under ethylene-oxygen and ether anesthesia. A "dilated stomach" was found, but no other intra-abdominal pathology. Later that morning the patient was in coma. Subsequently, she had an uninterrupted convalescence.

The difficulties presented to the surgeon in his attempt to differentiate abdominal pain due to impending coma, from impending coma due to a surgical lesion within the abdomen are such that it seems proper at this time to attempt to evaluate the various details of history, physical and laboratory findings from which he must make an ultimate decision.

Very little has been written about this subject. Apparently, no individual has had sufficient experience in the differentiation of these conditions to give any very definite criteria. We have, therefore, approached the subject by studying the cases reported in the literature, and by reviewing the records of the diabetic coma cases at the Massachusetts General Hospital, and the large series of cases placed at our disposal through the courtesy of Dr. E. P. Joslin.* The histories of emergency operations in diabetic patients under our own personal observation have been studied in detail. The findings in postmortem examinations of patients who have died in coma have also been utilized.

REPORTED CASES OF ASSOCIATED ABDOMINAL SYMPTOMS AND ACIDOSIS. Root in 1923 (Root, H. F.: *M. Clinics N. America,* 7: 641, 1923) in reporting a case of diabetic coma mentions "nausea and pains in the stomach". Joslin, Root, and White (Joslin, E. P.; Root, H. F., and White, P.: *M. Clinics of N. America,* 8: 1873, 1924) state that vomiting is a common symptom of acidosis occurring in more than one-third of the cases, and call attention to the fact that old blood is frequently present in the stomach. Ehrmann and Jacoby (Ehrmann, R., and Jacoby, A.: *Klin. Wchnschr.* 4: 2151, 1925) report a diabetic patient with acidosis, operated upon with a diagnosis of acute pancreatitis, with no pathology found at operation, and with negative findings at autopsy, except for a large quantity of blood in the stomach and intestines, and no obvious gastro-intestinal lesion to account for it. Allan (Allan, F. N.: *Am. J. M. Sc.* 174: 506, 1927) in discussing the leukocytosis which occurs in diabetic acidosis, mentions a nine year old girl who came to the Mayo Clinic with symptoms suggestive of appendicitis, but was not operated upon because appendicitis, if present, had gone on to general peritonitis. After twenty-four hours of insulin treatment, she was practically symptom-free. The white count in twenty-four hours dropped from 66,400 to 20,000.

Only a small number of cases have been reported where actual operation was done in the absence of demonstrable pathology. Obviously, the cases reported do not represent the number of operations which have been needlessly done. In table I are listed the cases we have been

*From the Massachusetts General and New England Deaconess Hospitals.

Read at the Annual Meeting of the New England Surgical Society at Boston, September 29, 1933.

†McKittrick — Surgeon-in-Chief, Palmer Memorial Hospital. Surgeon, New England Deaconess Hospital. For record and address of author see "This Week's Issue," page 1070.

*I am greatly indebted to Dr. Joslin and to his associates, Drs. Root, White, and Marble, for the inestimable help given by their personal discussion of each of the more important cases reviewed.

TABLE I

REPORTED CASES WITH DIABETIC ACIDOSIS AND NEGATIVE ABDOMINAL OPERATIONS

Author Reporting Case	Preoperative Diagnosis	Postoperative Diagnosis	Result
Ehrmann and Jacoby[1]	Acute pancreatitis	No pathology	Died
Usadel[2]	Perforated peptic ulcer	No pathology	Lived
Cabot Case Record[3]	Acute appendicitis with perforation	No pathology	Lived
Graham[4]	Gangrenous appendicitis	No pathology	Lived
Joslin[5]	Gangrenous appendicitis	No pathology	Died
Wheeler[6]	Emergency abdominal condition	No pathology	Lived
Author	Acute pancreatitis	Dilated stomach	Lived

[1]Ehrmann, R., and Jacoby, A.: Klin. Wchnschr. 4: 2151, 1925.
[2]Usadel, W.: Zentralbl. f. Chir. 54: 1364, 1927.
[3]Boston M. & S. J. 195: 1116, 1926.
[4]Graham, G.; Spooner, E. T. C., and Smith, W.: St. Bartholomew's Hosp. Reports. 62, 55, 1929.
[5]Joslin, E. P.; Root, H. F.; White, P.; Curtis, W. S., and Adams, H.: M. Clinics N. America. 13: 11, 1929.
[6]Wheeler, R. R.: Personal communication.

able to collect. It is interesting to note that in *each instance in which operation was done, the diagnosis was that of a widespread intra-abdominal calamity* rather than a definite, localized intra-abdominal process. Quite different is Joslin's case, No. 5732, who entered the hospital in coma, with no history of pain, recovered from coma only to die twenty-one days later. Autopsy showed an unsuspected appendix abscess as the cause of death.

CLINICAL FINDINGS IN COMA. A study of the records of patients in acidosis and coma with associated abdominal pain has brought out certain facts of clinical importance.

A careful history often reveals early symptoms of acidosis such as nausea, vomiting, diarrhea, and drowsiness preceding the onset of pain. This is noted in cases reported by Goldie (Goldie, W.: *Lancet*, 1: 301, 1933) and by Lawrence, Millman and Pilkinton (Lawrence, R. D.; Millman, C. G., and Pilkinton, F. E.: *Brit. M. J.* 2: 530, 1933). Rabinowitch (Rabinowitch, I. M., Macmillan Co., Toronto. P. 128, 1933) states that in "appendicitis, abdominal pain usually precedes vomiting, whereas in diabetic coma vomiting precedes the pain". While our own observations seem to bear this out, there were at least two patients with definite acute appendicitis at operation who had nausea and vomiting preceding pain.

The pain, usually in the upper, occasionally in the lower abdomen, may be intermittent or steady, and at times so severe as to cause the patient to writhe in agony. It may be accompanied by widespread spasm and tenderness. It is, however, *one of the first symptoms to disappear under insulin treatment*, there usually being marked improvement within a few hours.

A dilated stomach at times reaching enormous proportions, is common in coma. It may, not infrequently, give rise to upper abdominal symptoms. In one instance, definite peristaltic waves were noted. Hemorrhage, which may take place in such a dilated stomach, may be of clinical importance, as evidenced by Case No. 6649 (Joslin) that entered the hospital because she had "ruptured a blood vessel in her stomach". It is important to note, however, that the blood vomited in these cases is always dark, not the bright, freshly clotted blood such as is seen in bleeding ulcer.

The large fatty liver nearly always associated with diabetic coma is probably another cause of upper abdominal discomfort and tenderness.

Of the laboratory data, probably the most interesting is the almost constant leukocytosis. White blood counts of 30,000 to 40,000 per cubic millimeter are common. Case No. 8741 (Joslin) entered the hospital with a white blood count of 97,750. This dropped to 20,000 in twenty-four hours. This leukocytosis, like the pain, has not been satisfactorily explained. It responds promptly to insulin, although several days usually elapse before it becomes normal.

NECROPSY FINDINGS. Little help was obtained, in our present study, from the autopsy findings of coma cases. Much has been written about the importance of pancreatitis in diabetes, particularly when associated with diabetic coma. Of the 19 autopsies reported by Joslin, et al (Joslin, E. P.; Root, H. F.; Jordan, W.; White P., and Hunt, H.: *M. Clinics N. America*, 15: 829, 1932) there were three cases of acute pancreatitis with fat necrosis. Other cases of acute pancreatitis reported (Bayer, L.: *Am. J. M. Sc.* 179: 671, 1930; Foord, A. G., and Bowen, B. D.: *Am. J. M. Sc.* 180: 676, 1930; Gibb, W. F., and Logan, V. C.: *Arch. Int. Med.* 43: 376, 1929) suggest that an acute pancreatitis is not an infrequent occurrence in diabetes, although as Joslin (Joslin, E. P.; Root, H. F., and White, P.: *M. Clinics N. America*, 10: 1281, 1927) suggests, the pancreatitis is the probable cause of coma and not the result of it.

To explain the abdominal symptoms associated with diabetic acidosis on the premises of either the clinical or the operative findings, or on the findings at autopsy, is impossible. It has been suggested by Schöndube (Schöndube, *Deutsche. Med. Wchnschr.* 56: 183, 1930) that the spasm of the abdominal wall and intra-abdominal pain, and peritoneal symptoms are explained by the deprivation of water in the tissues. Warfield (Warfield, L. M.: *J. A. M. A.* 89: 654, 1927) has suggested that it is due to a pancreatitis. The absence of gross evidence of pancreatitis in the cases operated upon and, particularly, the marked rapidity with which the pain subsides by treatment with insulin argues strongly against this explanation.

EMERGENCY OPERATIONS UPON CASES WITH DIABETES. In table II are listed the emergency abdominal operations which have come under our observation. A diagnosis of acute appendicitis was made 23 times and of perforated duodenal ulcer once. In each case a definite history of abdominal pain and associated tenderness, with or without muscle spasm, seemed to the writer to warrant this diagnosis and an emergency operation, in spite of the fact that ten process in relation to the appendix would still be found. In two of these cases no definite explanation for pain could be discovered at operation. In the third case there was definite tabes mesenterica. None of the three patients had any evidence of a recent inflammatory process in the abdomen.

In going over these cases, analyzing the histories and physical findings, one is impressed by the fact that the findings from which the sur-

TABLE II

EMERGENCY OPERATIONS UPON PATIENTS WITH DIABETES MELLITUS WITH OR WITHOUT ACIDOSIS

Case No.	Age	Temp.	WBC	Diacetic Acid	Preoperative Diagnosis	Postoperative Diagnosis	Result
1	18	101	15,950	++++	Ac. append., abscess	The same	Relieved[1]
2	7	103 (r)	6,450	0	Ac. append.	The same	Relieved
3	51	100[2]	18,200	0	Ac. append.	The same	Relieved
4	37	100[4]	13,300	0	Ac. append.	Ac. gangrenous append.	Relieved
5	29	98[6]	?	0	Ac. append.	Ac. append.	Relieved
6	65	98[6]	?	?	Appendix abscess	The same	Relieved
7	12	100	18,100	0	Ac. appendicitis	The same	Relieved
8	23	101	15,000	+++	Ac. appendicitis	Ac. regional ileitis[2]	Relieved
9	58	98	?	0	Spreading peritonitis, probably from append.	The same	Died
10	9	101 (r)	25,000	+	Ac. appendicitis	The same	Relieved
11	13	100[4]	23,800	++	Ac. appendicitis	Ac. gangrenous append.	Relieved
12	14	100	14,000	0	Ac. appendicitis	The same	Relieved
13	17	99[2]	19,650	++	Ac. appendicitis	The same	Relieved
14[3]	38	99	18,500	++++	Ac. appendicitis	The same	Relieved
15[4]	15	99[8]	13,800	0	Ac. appendicitis	The same	Relieved
16	54	100[8]	25,000	++++	Ac. retrocecal append.	Inflammatory process ard. lower pole of kidney	Relieved
17	54	101	24,500	+	Spreading peritonitis, sec. to appendicitis	The same	Relieved
18	33	100[4]	10,960	0	Ac. appendicitis	Tabes mesenterica	Relieved
19	61	100[4]	15,500	0	Ac. appendicitis	Ac. gangrenous append.	Relieved
20	41	99[8]	14,200	?	Ac. appendicitis	Ac. gangrenous append.	Relieved
21	44	100[6]	22,000	+++	Ac. appendicitis	Ac. salpingitis	Relieved
22	55	99[4]	15,000	++++	Perf. duodenal ulcer	The same	Relieved
23	15	99	20,000	0	Ac. appendicitis	The same	Relieved
24	44	98[6]	13,950	+	Ac. appendicitis ? beginning abscess	Ac. gangrenous append.	Relieved

[1]Abscess drained. Returned 3 months later and appendectomy done.
[2]Terminal ileum. 12 cm. swollen, edematous with flecks of fibrin on serosa.
[3]Operation by Dr. R. H. Sweet.
[4]Operation by Dr. T. C. Pratt.

of the patients had definite acidosis. There were four mistakes in diagnosis: one case diagnosed as acute appendicitis proved to be acute salpingitis; another had an acute regional ileitis involving a segment of terminal ileum approximately six inches in length; a third had an acutely inflamed gland in the mesentery of the terminal ileum, and in the fourth case there was an inflammatory process involving the lower pole of the right kidney instead of a retrocecal appendicitis.

In addition to this series of cases, three children were deliberately operated upon after repeated attacks of abdominal pain associated with acidosis; all of them were seen by the writer during the attacks, and in no instance were the signs and symptoms sufficiently definite to warrant a diagnosis of appendicitis, or of any other definite intra-abdominal lesion. These children were operated upon, not as emergencies but following treatment of their acidosis, and sufficiently soon after the onset of acute symptoms, so that evidence of any inflammatory geon is accustomed to make a diagnosis of acute appendicitis are present in the diabetic patient, whether he has acidosis or not. It is of no little importance to note, however, that the signs and symptoms may be masked by the diabetes and acidosis rather than exaggerated, and that one makes such a diagnosis not upon the widespread signs and symptoms of an abdominal calamity but upon less than the usual local tenderness and spasm.

SUMMARY. From what has been said certain important facts stand out.

(1) In all cases operated upon with negative findings, a diagnosis of an extensive surgical lesion, such as acute pancreatitis, general peritonitis, or perforated ulcer has been made.

(2) In all cases of our series where a diagnosis of acute appendicitis was made, whether acidosis was present or not, a history of pain, associated with localized tenderness and spasm was found. It is, however, true that the degree of spasm and tenderness was, if anything, less

marked in this group of diabetic patients than in corresponding patients without diabetes.

(3) A history carefully taken from the family if not possible from the patient suggests that in many cases without demonstrable lesions the early symptoms are those of coma which precede the onset of pain, rather than a definite history of abdominal pain suggesting a surgical lesion, which is the cause of the acidosis and coma. Thus, Smith (Smith, J. H.: *J. A. M. A.* 92:308, 1929) reports a case of "unmistakable signs of appendicitis" which, because of a previous experience, was diagnosed as being due to diabetic acidosis. This same patient returned at a later time with the same symptoms. An acutely inflamed appendix was found.

(4) Just as severe abdominal pain may be the outstanding symptom of a patient with impending coma, it is the first symptom to disappear under proper insulin treatment. Whereas, with a definite intra-abdominal lesion present causing the pain, it will persist or increase in spite of treatment for the acidosis. This is confirmed by the case of Scherk (Scherk, G.: *Deutsche. Med. Wchnschr.* 55:1878, 1929) whose patient had severe abdominal pain, associated with coma which increased rather than diminished as the coma cleared. Autopsy, in this instance, showed a thrombosis of the celiac artery. Crecelius (Crecelius, W.: *Klin. Wchnschr.* 8:878, 1929) feels strongly that the progress of symptoms under diabetic treatment is of great help as evidenced by his patient with definite abdominal symptoms and leukocytosis. The leukocytosis increased in spite of insulin treatment and at operation a perforated appendix was found.

From the above facts, one is justified in saying that a history of malaise, drowsiness, vomiting, diffuse abdominal pain, associated with widespread tenderness and spasm is so suggestive of diabetic acidosis, without demonstrable intra-abdominal pathology that operation should not be done unless the abdominal symptoms persist after three or four hours of adequate insulin treatment. Conversely, a history of abdominal pain with or without vomiting, when associated with localized and definite abdominal tenderness, usually with spasm, is suggestive of a surgical lesion within the abdomen in the patient with diabetic acidosis, just as it is in the non-diabetic, and may be an indication for immediate operation. In that rare case, where definite differentiation is impossible and yet imperative, it may be safer to open the abdomen under local anesthesia than to suffer further delay.

DISCUSSION

DR. WALTER C. SEELYE, Worcester, Mass.: I have been very much impressed by Dr. McKittrick's paper on the subject of acidosis and diabetic conditions associated with acute abdominal symptoms and I think that we should all derive a great deal of profit from what he says with respect to these cases, and avoid unnecessary laparotomies in those cases which seem like desperate, acute abdominal lesions upon their admission to the hospital.

The emphasis which he places upon the differential diagnosis, I think is very beautifully brought out, and the facts which impressed me particularly are those of not being in a hurry although the case may seem desperately sick. A few hours' delay will not jeopardize the patient, and treatment with insulin and a little further observation will often save us from operating on a case where we felt at first there was a definite abdominal lesion.

I think also that a careful history which would lead us to suspect that the abdominal condition is due to acidosis and a diabetic condition, is most important in these cases.

My experience has been practically nil in these cases but has dealt mostly with adults that had definite abdominal lesions with diabetes. I do feel, however, that we as surgeons, when confronted with emergencies of this sort, must get all the help that we can. A consultation with the diabetic experts would help us in verifying these cases before we enter the abdomen and that is a very important consideration.

DR. STEPHEN A. MAHONEY, Holyoke, Mass.: There is one case I should like to report relative to diabetes in a fifteen year old girl. She prides herself on being practically the first case to whom Dr. Joslin ever gave insulin. The mother, who has been constantly giving her insulin, three times a day for the past nine years, thought she knew everything, every angle and crook that diabetes could bring on. The child awakened one morning with a severe abdominal pain. She has had this pain many times before and the mother considered it was simply one of the abdominal pains that go with acidosis; therefore, she did not call upon her son, who is an associate of mine, to examine the child. The doctor was away for the day and it was thirty-six hours before he saw the case.

There were a few symptoms in it that differed from the ordinary abdominal pain that goes with acidosis, and he asked me to see the case in consultation with him. Knowing nothing about diabetes or abdominal pain, or anything else in acidosis, the picture was one to me of absolute acute appendicitis and I advised immediate operation. They consented against the mother's advice and judgment, because she thought she knew so much about diabetes from her long-continued treatment of it, but we went into the abdomen and found a ruptured appendix that evidently had been ruptured four or five hours. After an exceedingly stormy convalescence, in which at times the blood sugar ran up as high as 400 and there was constant sugar in the urine, the child recovered. When you are dealing with abdominal pain in diabetes, I think, as Dr. McKittrick says, that you should treat the patients just as if they did not have diabetes.

THE NEW HAMPSHIRE MEDICAL SOCIETY

SYMPOSIUM
DISEASES OF THE BILIARY TRACT—DIAGNOSIS AND TREATMENT*

Medical Aspects

BY REGINALD FITZ, M.D.,† BOSTON

Mr. President and Members of the New Hampshire Medical Society:

IN the first place I must thank you for allowing me this chance to attend a meeting of this State Society. In the second place, I must state how deeply I appreciate the honor of being on a program in company with Dr. George W. Holmes, Dr. Alfred T. Bazin and Dr. Frank H. Lahey. In the third place, I must congratulate you on the choice of topic which you have selected for discussion. All diseases of the Biliary Tract present difficult problems in diagnosis and treatment and the great majority, at one time or another, form a common meeting ground for the medical man, the radiologist and the surgeon. Today I have the advantage of position, for in the management of such cases the medical man, usually, is the first doctor to see the patient.

Let us imagine that before us there now appears a man fifty years old, who says that he has "the yellow jaundice". He wishes to know what is wrong to make him of this color and what can be done about it.

Two questions at once flash across our minds: Has this patient an *obstructive* type of jaundice or not, and has he a type of jaundice best treated by *surgery* or otherwise? To a great extent, proper therapy will depend on our ability to answer these questions correctly.

Most skilful clinical teachers agree that in dealing with jaundiced cases what the patient says is the most important step in diagnosis; next what the physical examination reveals; that the laboratory findings are relatively insignificant; and that the x-ray, at times, may be misleading. Hence a good history is essential.

Is the jaundice acute or chronic? Is it persistent or intermittent? Is it increasing or decreasing in intensity? Is it painful at all, and if so to what region is the pain referred? It is worth remembering that nearly a third of the patients with gall-bladder disease complain of left-sided pain. Some may refer their pain to the mid-back. The classical textbook story of gall-bladder colic is comparatively uncommon; intermittent upper abdominal pain is always suggestive.

Another point to be investigated carefully deals with the question of fever. Has the patient been conscious of chilly feelings or even of true shaking chills from time to time? Charcot's intermittent type of hepatic fever is very important to recognize, signifying so often a common duct stone with intermittent obstruction of the common duct and infection above the point of obstruction.

A third point deals with the matter of drugs. Has the patient taken any medicine that might provoke jaundice? Beware of the possibility of liver poisoning from cinchophen and its derivatives. Remember that arsenic may produce toxic hepatitis and that alcoholic cirrhosis, still, is by no means uncommon.

Has the patient lost weight? Loss of weight is always significant. Even the mildest catarrhal jaundice will produce enough loss of appetite and malaise to induce some weight loss. The point we are after, however, is to determine whether the patient has been losing weight insidiously over a long period of time with the jaundice an additional thinning factor; or whether the weight loss has been acute and coincidental to the jaundice. Along with this question we well may ask the patient what he has to say about the size of his abdomen. He may reply that he has noticed a very peculiar thing; he has become noticeably thin in his arms and legs, yet he has held his weight or even gained a few pounds and has developed a pronounced bay window. In fact his friends have made fun of his appearance suggesting that before long most likely he will be having twins. This statement is very significant, suggesting either an accumulating ascites or great overgrowth of liver tissue.

What about the appetite and digestion? Has the patient had much nausea and vomiting and particularly has he vomited blood? Are the stools clay white, tarry, or about of normal color? Persistent common duct obstruction, of course, will always be accompanied by clay colored stools, while intrahepatic jaundice may produce no gross change in the color of the stools whatever. Finally, as in all cases of gastrointestinal disease with jaundice, it is important to remember that the liver may be the site of secondary cancer; hence the history of intermittent diarrhoea and constipation or of any form of indigestion may be most important.

Itching of the skin usually suggests long-standing jaundice. When a middle-aged per-

*Read at the Annual Meeting of the New Hampshire Medical Society at Manchester, May 17, 1933.

†Fitz—Physician to Peter Bent Brigham Hospital, Boston. For record and address of author see "This Week's Issue," page 1070.

son complains of generalized itching one should at once suspect the existence of biliary disease or of Hodgkin's Disease.

Next in importance to a good history is a thorough physical examination. In cases with jaundice there are certain points to be examined with especial care. Be sure to feel for enlarged glands. Medical men on the whole prefer, apparently, to hear or see things rather than to feel them. Feel above the clavicles. A firm gland above the left clavicle suggests cancer of the stomach; one on the right side is more suggestive of Hodgkin's Disease or of a mediastinal or pulmonary neoplasm. Feel carefully around the umbilicus, in the axillae and groins, and even over the sacrum for here occasionally a metastatic nodule is encountered. Always make a rectal examination. Feel the prostate for nodules, in the region of the seminal vesicle for infiltration, at the rectosigmoid for a primary growth and on the rectal shelf for metastases. A metastasis on the rectal shelf can be discovered in no other way than by palpation.

An enlarged liver is fairly easily felt; it is reasonably easy, too, to determine whether the liver is of firmer than normal consistency and, at times, whether it is nodular. It is also possible to determine whether the liver is abnormally small. An enlarged gall bladder may be palpable. In the presence of complete jaundice, a palpable gall bladder is very suggestive of cancer of the head of the pancreas. An enlarged spleen is likely to occur in cirrhosis of the liver; an enlarged left lobe of the liver in syphilis. At times it may be difficult to tell the difference between an enlarged left lobe of the liver and an enlarged spleen, but at least one should attempt to make the distinction.

A large ascites is easily recognizable. Personally, I find it difficult to detect with sureness small accumulations of fluid in the peritoneal cavity. However, certainly, one should attempt to elicit the signs of shifting dullness, for in biliary tract disease free fluid in the peritoneal cavity is significant, and its presence may have much to do with the form of treatment instituted. Edema of the legs or general anasarca, too, are significant findings. The jaundiced patient with general anasarca never makes a good operative risk.

Laboratory studies, in general, are not overhelpful in the diagnosis of the cause of jaundice. Remember, however, that the blood count may be important. Jaundice will quickly produce a moderate degree of anemia but never, without serious hemorrhage, so low a red blood count as occurs in pernicious anemia. Pernicious anemia may produce a very yellow-looking person yet such jaundice is not obstructive in origin, and is never benefited by surgery. Thus in a patient with jaundice and anemia it is important to exclude pernicious anemia. One must be on the lookout, too, for that very peculiar type of jaundice and anemia known as hemolytic jaundice wherein the red cells are unduly fragile. Here, again, one encounters jaundiced and anemic patients, without bile in the urine, with normal colored stools and usually with a palpable spleen. Often such cases have gallstones as well. In hemolytic jaundice the red cells *in vitro* will be hemolysed more easily than normal cells. In this particular group the laboratory is very useful, for if the cases are recognized they may be helped wonderfully by splenectomy.

Many cases of jaundice must be observed for considerable periods of time before it becomes clear as to their best treatment. In following an individual case, it is important to note the color of the stools from day to day. The appearance of the skin may change; the jaundice may appear to be diminishing, yet no bile may be forthcoming in the stool, an ominous sign suggesting failure of liver function. On the other hand, do not be misled by other pigments than bile which may produce colored stools. Iron or bismuth will produce black stools. I well remember as a house-officer having an attack of catarrhal jaundice and how optimistically a cascara-tinted stool made me feel only to be followed by dark melancholy when clay colored movements again occurred after the drug was omitted.

Certain observers lay stress on the diagnostic value of an examination of the duodenal contents according to the Meltzer-Lyon method. With this method, personally, I have had no luck. The Wassermann reaction, too, may give misleading information. In jaundice, false positive readings may be obtained and this is an important fact to bear in mind since arsenic wrongly applied to a damaged liver may prove an irreparable insult.

Every patient with persistent jaundice has a right to surgical consultation. The surgeon will wish to know what the blood, urine, and stools show in addition to what he elicits from history taking and physical examination. He may wish to know whether the patient's bleeding or coagulation time is abnormal and something, too, of the blood chemistry. Liver function tests, on the whole, are not very helpful. If the patient has an obstructive jaundice one knows that liver function is disturbed. In cases of biliary system disease without jaundice, on the other hand, tests for liver function may be valuable.

The medical treatment of jaundice, excluding pernicious anemia and syphilis, is not very fruitful. The patient may need rest and observation; he should be given an easily digested diet containing an abundance of sugar. If he has ascites, he may derive almost dramatic

benefit from repeated courses of ammonium chloride and salyrgan, and may thus escape the potential dangers of repeated tappings.

Thus the fifty year old man now before us with "the yellow jaundice" has many possible reasons for feeling out of sorts and several possibilities regarding what can be done about it. At this juncture I feel urgently in need of help and beg for assistance from the keen-sighted radiological eyes of Dr. Holmes and the skilful surgical hands of Dr. Bazin and Dr. Lahey.

THE ROENTGEN EXAMINATION OF THE GALL BLADDER*

BY GEORGE W. HOLMES, M.D.†

CARL BECK of New York is usually credited with being the first to demonstrate gall stones in a living subject. His work was published in the *New York Medical Journal* in 1900. Buxbaum of Karlsbad undoubtedly preceded Beck by two years; out of thirty attempts on living subjects he demonstrated stones in four cases.

Following these early reports repeated attempts were made to demonstrate gall stones, and with improvement in apparatus and photographic material considerable success was obtained; the degree of success depending largely upon the amount of lime salts in the stones studied and the perfection of the radiographic technique, since only about thirty per cent of all gall stones contain sufficient lime salts to render them visible on the x-ray film, negative findings were of little value. This method of examination was also of no value in cholecystitis without stones, which is the condition present in a considerable portion of patients suffering from gall bladder disease.

Following the introduction and general use of the opaque meal, as a means of examining the gastro-intestinal tract, certain changes in the contour of the stomach or duodenum, or of their muscular activities were seen which could not be attributed to intrinsic lesions. Further investigations of these phenomena led to the discovery of the so-called indirect signs of gall bladder disease. Schürmayer studied the effect of adhesions upon the stomach and duodenum and reported his findings in 1910. Probably the first in this country to call attention to the value of these signs in the diagnosis of gall bladder disease was George Pfahler of Philadelphia, at about the same time Cole of New York and George of Boston published their observations on the value of indirect signs. Gall bladder examination was brought to a high degree of perfection by Case, Cole, George and Leonard and consisted of the demonstration of stone, when possible, known as the direct signs; and a study of the gastro-intestinal tract with the opaque meal to demonstrate the presence or absence of pressure deformities, changes in peristalsis or displacements, the so-called indirect signs. This method, although satisfactory in the hands of experts, was never generally used. The possibility of error was too great; a high percentage of stones failed to visualize, many diseased gall bladders failed to show the indirect evidence of disease; this was particularly true of the early cases, and was occasionally true in cases with extensive adhesions, and gall bladder radiography was of limited value to the surgeon. This dissatisfaction led to attempts to render the gall bladder visible by other means, and in 1923 Graham and Cole conceived the idea that the gall bladder could be made visible to the roentgen ray by filling with a contrast substance, secreted by the liver. If this could be accomplished not only would pathological changes in that organ be recognized earlier but such a procedure would give an accurate index of function of both liver and gall bladder. It is largely due to their epoch-making work that the present high degree of accuracy in gall bladder diagnosis has been obtained.

The method which Graham and Cole developed embodies an entirely new and original radiological prineiple, namely, the utilization of the specific functions of a system or organ to bring about a difference in density. Cholecystography is, therefore, largely a test of physiological function in contradistinction to the almost wholly anatomical nature of the examination of the gastro-intestinal tract with the opaque meal. Briefly, the method consists of the introduction into the body either through the blood stream or the gastro-intestinal tract of a non-toxic preparation of iodine, tetraiodophenolphthalein, which is secreted by the liver and concentrated in the gall bladder causing it to become visible on the roentgen film. The intravenous method was the one first described by Graham and Cole and is still used and advocated by them.

The oral method was first demonstrated in this country at the Peter Bent Brigham Hospital by Sosman and Whitaker, and has since become the method generally used. Kirklin of the Mayo Clinic, in a paper read before the American Radiological Society proved beyond a doubt that this method, when properly used is as accurate as the intravenous method. Since it is

*From the Roentgenological Department—Massachusetts General Hospital, Boston, Massachusetts.
Read at the Annual Meeting of the New Hampshire Medical Society at Manchester, May 17, 1933.

†Holmes — Roentgenologist, Massachusetts General Hospital. For record and address of author see "This Week's Issue," page 1070.

much simpler and more easily carried out, it is now the method generally used and is the one which I will discuss here.

Accuracy with the oral method depends largely upon three factors: first, the selection of a fresh active sample of the dye, in a form which can be easily absorbed from the gastro-intestinal tract; secondly, the administration of the dye at the proper time in relation to the intake of food; and thirdly, a routine procedure of examination which results in radiographs of the highest technical quality. Fortunately, through the efforts of the large chemical houses, the drug is now available under trade names in excellent form for oral administration and the difficulty of securing it fresh and in a proper form has largely been eliminated. Any of the preparations now on the market are satisfactory. Excellent rules for the administration of the drug have been published by Kirklin, and I can do no better than to quote him:

1. It should be administrated in sufficient quantity and in freely absorbable form.
2. It should be so given that it will not tend to excite nausea, vomiting or annoying catharsis.
3. It should be taken into the stomach immediately after the ingestion of a full meal containing a minimal quantity of fats.
4. Fats should be withheld subsequently until the gall bladder has had an opportunity to fill with dye-laden bile and to concentrate it.
5. As a routine, roentgenograms should be made at not less than three properly spaced intervals.
6. A fatty meal between the final sets of roentgenograms is essential.
7. Other foods or drink that might empty the gall bladder prematurely should not be taken by the patient.
8. Purgatives and other medicaments that may affect the motility or absorbability of the bowel or the function of the gall bladder are to be interdicted during the period of examination.

This procedure has been satisfactorily employed at the Mayo Clinic for a number of years, and in general is the procedure used at the Massachusetts General Hospital. It is of the greatest importance that these rules be adhered to; since an error in carrying them out may result in a positive where a negative diagnosis should have been made. For this reason we have added a follow-up sheet on which is recorded the symptoms of which the patient complained, the hours at which the drug was taken, and at which the examination was made; also a statement as to whether the patient vomited or took food during the interval between the taking of the drug and the making of the examination. These data are obtained from the patient by the technician at the time the examination is made and have essentially reduced the number of diagnostic errors, due to failure to carry out the proper technique of administrating the dye.

MASSACHUSETTS GENERAL HOSPITAL

X-RAY DEPARTMENT GALL BLADDER SHEET

Name.....Age.....Date.....X-Ray No. .....

Clinical Diagnosis.....Service.....O. P. D. No. .....

History.....House No. .....

.....

.....

.....

Dye Used and Amount.....

Hour Given.....Hour Examined.....

Number of Films Taken.....

Interval History and Food Taken.....

.....

.....

.....

X-Ray Findings.....

.....

.....

.....

.....

Follow Up History.....

.....

.....

.....

Abstinence from fat-containing food is of equal importance whether the oral or intravenous method is used; since a positive diagnosis is based on failure of the gall-bladder to become visible and may be due either to disease of the gall bladder or to emptying of the gall bladder from the improper taking of food. The improper taking of food or failure to take a sufficient amount of the dye is properly the most common source of error in gall bladder diagnosis at the present time. It is our custom to give the dye immediately following the evening meal which should be fat free, the first observation being made the following morning or about sixteen hours after the ingestion of the dye. The exact time is not important providing no food is taken and a sufficient time has elapsed. The exposure is made with the patient prone upon the examining table, the tube is centered over the gall bladder region, at a distance of about thirty inches from the film; the Bucky diaphragm is used and the exposure is made as short as is consistent with obtaining a radiograph of sufficient contrast; the exposure time will depend largely upon the apparatus used. The shorter the exposure, the less danger there is of motion and consequent blurring of the film. The resulting radiograph should show the bony structure of the ribs, and a sharp clean cut outline of the gall bladder and lower margin of the liver; since the gall bladder may lie anywhere between the eleventh rib and the crest of the ilium, close to the spine or well out

toward the periphery of the abdomen, it is essential that the film include this area at least. When routine films fail to show the gall bladder it is necessary to explore beyond this area; a search should be made as high as the diaphragm, behind the spine, over the psoas muscle, and as low as the pelvic brim. Repeating the film at a later hour has not, in our experience, added anything to the diagnosis. If the gall bladder fails to fill in sixteen hours, it in all probability is diseased provided the technique has been properly carried out. There are two exceptions to this statement; first, a badly diseased liver which fails to secrete the dye; and secondly, when the oral method is used, obstruction at the pyloric orifice. Before making the exposures the patient should be instructed to remain quiet on the table and to stop breathing; usually it is desirable to take films at both inspiration and expiration, as the movement of the gall bladder during the respiratory cycle may help to distinguish non-opaque stones from small gas bubbles in the duodenum or colon.

After the preliminary examination has been made, the patient is instructed to take a meal containing fat or egg yolk and to report within one hour for the second observation. The period of time between the first and second observation will depend somewhat upon the data which is to be obtained; if non-opaque stones or tumor are suspected in the first observation it is desirable to make the second before the gall bladder is completely empty. Examination during the emptying period may also demonstrate the common and cystic ducts. Where complete emptying is desired the longer time should be used. We have not found it necessary to make an examination at the end of the twenty-four hour period. In all cases in which the roentgen findings are inconclusive or in which they disagree with the clinical findings, the examination should be repeated. When repeating the examination it is not necessary, in our opinion, to use the intravenous method, a second oral examination being equally satisfactory.

Ferguson and Palmer have recently studied the results obtained from 2070 cholecystographic examinations to determine the accuracy of the various findings and conclude that:

1. A good visualization of the gall bladder cholecystography with no evidence of stones indicates a normal gall bladder in a very high percentage of the cases. Exact figures as to its accuracy are difficult to give.
2. The accuracy of diagnosis when stones are demonstrated as positive or negative shadows approaches 100 per cent.
3. The accuracy of a faint visualization, when combined with a clinical history suggestive of biliary disease, is 58.3 per cent; that of nonvisualization when combined with a positive clinical history, 90 per cent.
4. In the absence of a clinical history suggestive of gall bladder disease, the accuracy of a faint visualization is less than 14 per cent; that of nonvisualization considerably less than 66.6 per cent.

In my opinion this statement of Ferguson and Palmer is a fair estimate of the value of the roentgen findings in the diagnosis of gall bladder disease.

CONCLUSIONS

In conclusion, one may state that the present roentgen method of examining the gall bladder gives accurate results in a high percentage of cases, not only as to the presence or absence of gall stones, but also to the presence or absence of a non-functioning gall bladder; in a certain small percentage of cases, a diseased gall bladder without stones may function well enough to give a negative test. In other words, negative roentgen findings do not rule out gall bladder disease. The technique is reasonably simple and possible to carry out in any well-conducted clinic. It does require considerable care with special attention to detail. There are no contraindications in so far as danger to the patient is concerned. The test is usually positive, that is, the gall bladder is not visualized in patients with jaundice or those with extensive malignant disease of the liver or pancreas and is of little diagnostic value in these cases. For this reason the presence of jaundice is often given as a contraindication to the use of the method.

Statistical reports of the accuracy of any method of diagnosis are often misleading when applied to a given case or clinic; nevertheless, they sometimes serve to emphasize the importance of the various findings on which the diagnosis is based.

REFERENCES

Beck, Carl: On the detection of calculi in the liver and gall-bladder. New York M. J. 71: 73, 1900.

Buxbaum, A.: Ueber die Photographie von Gallensteinen in vivo. Wien. Med. Presse. 39: 534, 1898.

Case, J. T.: The relative value of cholecystography and the so-called direct and indirect methods of roentgenological examination of the gall-bladder. Am. J. Roentgenol. 16: 238, 1926.

Cole, L. G.: The detection of pure cholesterine gall-stones by the roentgen rays. Am. J. Roentgenol. 1-2: 640, 1913-1915.

Ferguson, A. N., and Palmer, W. L.: Cholecystography: Its clinical evaluation. A study of 2,070 cases. J. A. M. A. 100: 809 (March) 1933.

George, A. W., and Leonard, R. D.: The roentgen diagnosis of a pathological gall-bladder. Am. J. Roentgenol. 4: 321, 1917.

Graham, E. A., and Cole, W. H.: Roentgenologic examination of the gall-bladder. Preliminary report of a new method utilizing intravenous injection of tetrabromphenolphthalein. J. A. M. A. 82: 613, 1924.

Pfahler, G. E.: Gastric and duodenal adhesions in the gall-bladder region, and their diagnosis by the roentgen rays. J. A. M. A. 56: 1777, 1911.

Schürmayer, C. B.: Pathologische fixation bzw. Lagveränderung bei Abdominalorganen und die röntgenologische diagnosestellung. Fortschr. a. d. Geb. der Röntgenstrahlen. 15: 317, 1910.

Sosman, M. C.; Whitaker, L. R., and Edson, P. J.: Clinical and experimental cholecystography. Am. J. Roentgenol. 14: 495, 1925.

Kirklin, B. R.: Necessity for accurate technique in oral cholecystography. Errors attributable to technical lapses. Am. J. Roentgenol. 25: 595, 1931.

SURGICAL ASPECT OF DISEASES OF THE BILIARY TRACT*

BY A. T. BAZIN, M.D.,† MONTREAL

A SYMPOSIUM on any subject is apt to be difficult for both speakers and audience. Unless the team to present the subject is drawn from a body of co-workers who consult frequently in preparing the component parts, there is apt to be a lack of meshing of the gears, or a tiresome overlapping.

In March Dr. Fitz and I corresponded in an endeavor to correlate, and therefore I am going to limit my remarks to a discussion of certain surgical problems that constantly arise.

Infection is the most common and therefore the most important of the diseases of the biliary tract.

The infection may be present with or without stones, may be limited to the gall bladder, or diffused throughout the biliary tract including the liver, or spread to related organs, such as the pancreas more especially.

The inflammatory reaction may be acute from the beginning (notably in typhoid cholecystitis) or chronic throughout its course, or chronic with acute exacerbations.

The presence of gall stones predicates with one exception the association or preëxistence of some degree of infection.

The exception is in hemolytic jaundice where multiple pigment stones are found in 80 per cent of such cases. Even here there may be an accidentally associated infection from which symptoms will persist even after splenectomy for the blood dyscrasia and removal of the gall stones, leaving what is apparently a healthy gall bladder.

Gall stones may mechanically produce symptoms of colic or of obstructive jaundice, and with absence or but a modicum of the signs of infection.

With such protean possibilities in pathological or abnormal conditions, it behooves us to use studied judgment in interpreting signs and symptoms.

The problem of Acute Cholecystitis is when to operate and how much to do.

The treatment of the acute gall bladder has been likened to that of the acute appendix, viz., operate as soon as diagnosed.

This, as with most attempts to standardize treatment, is in my opinion a mistake.

The limitations of safe operative interference in the presence of acute infection are very definite. Simple drainage with removal of stones if present, or simple cholecystectomy, or drainage of both gall bladder and pericholecystic abscess is the extent of safe operative procedure.

In many instances there will remain conditions of a diffused chronic infection which for their relief will require a second operation under increased difficulties of adhesions and distortion of anatomic relations.

To attempt to do common duct exploration and drainage in the presence of such acute infection is to invite disaster. For the common duct cannot be reached without incising the peritoneum of the gastrohepatic omentum, and the fatty and areolar tissue between its leaves communicate directly with the similar tissue in the retroperitoneal space and a retroperitoneal phlegmon may result.

Therefore it is wise to temporize with a case of acute cholecystitis, permit of subsidence of the acute symptoms and signs, study the patient for evidence of a more diffuse biliary infection and be prepared to operate adequately as in any case of chronic cholecystitis (vide infra).

Throughout the attack careful watch must be kept lest the disease pass beyond the confines of the gall bladder wall. An increasing tenderness, an increasing rigidity of the overlying muscle or an increasing area of the rigidity, the development of acute rebound pain, recurring chills, etc., are indications that acute empyema of the gall bladder is present or that the infection has extended through the wall either by gross rupture or bacterial invasion.

Under such circumstances delay is no longer justified; a life-saving drainage operation must be done at once.

The chronic case with acute exacerbations seldom fails to subside under appropriate treatment.

It is the case which is acute with the first attack that is more likely to progress in the above manner. Typical of this class is the acute typhoid cholecystitis.

Some of us can remember the days of typhoid fever as a prevalent disease. There are few of us who do not occasionally see a case.

Cholecystitis as a complication of the third week of the fever is not uncommon, in fact it is the most common surgical complication next to perforation.

The means of diagnosis and method of treatment depend entirely upon the state of the patient.

With the patient mentally alert and responsive to pain reflexes there will be not only alteration in temperature chart and white blood count, but there will be complaint of pain and tenderness over the gall bladder. In such pa-

*Read at the Annual Meeting of the New Hampshire Medical Society at Manchester, May 17, 1933.

†Bazin—Professor of Surgery, McGill University. For record and address of author see "This Week's Issue," page 1070.

tients the condition may be watched and tided over to convalescence. Invariably the gall bladder should be removed when convalescence is established and before the individual is permitted to rejoin society, as these patients are always "carriers" until cholecystectomy is performed.

But the typhoid patient in a state of torpor and apathy may have a cholecystitis which may go on to rupture, peritonitis and death without a complaint on his part.

Here the diagnosis is based upon the finding of some vague tenderness, possibly muscle resistance, in the course of the daily routine examination of the abdomen. The distended gall bladder may be defined. Usually there will be also a leucocytosis.

In this type of patient operate at once. Under local anesthesia do a simple drainage of the gall bladder. Seldom are there any stones. If there are, they were preëxistent.

THE PROBLEM OF CHRONIC CHOLECYSTITIS

I do not like this term. I would rather it were superseded by the term Chronic Biliary Infection.

I believe that if we approach every case with the suspicion that the infection is diffuse rather than limited to the gall bladder, we will be prepared to give more adequate treatment and to leave much fewer cases with a postoperative aftermath of symptoms.

I do not refer to those patients with undoubted implication of the common duct as evidenced by jaundice or Charcot's intermittent fever, nor to such associated conditions as peptic ulcer or chronic appendicitis. In all laparotomies for chronic biliary infection a careful exploration of the whole abdomen should be done and such associated conditions discovered and treated.

If preoperative study reveals a defective hepatic function or operation discloses the signs of a recent or remote diffuse hepatitis, the common duct should be opened and explored.

If the blood sugar time curve reveals a pancreatic dysfunction or operation discloses structural change in the pancreas, the common duct should be opened and explored.

If palpation or inspection reveals thickened or dilated extrahepatic ducts the common duct should be opened and explored.

Palpation of the common duct fails in many instances to reveal stones or bile mud which are proved to be present when the common duct is opened.

Routine exploration of the common duct consists of:

1. Introduction of ureteral stone forceps if the duct is sufficiently dilated.

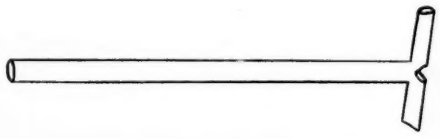
2. Passage of a probe into the duodenum followed by a graded dilation of the ampulla by means of Van Buren sounds up to the capacity of the duct.

3. Through and through irrigation of the duct with normal saline.

Drainage of the duct, with associated suture for repair, should, in my opinion, always be done by means of a T tube. This allows tight closure against bile leakage into the peritoneal cavity and obviates the danger of contraction of the duct with subsequent stricture. The T tube allows of restoration of the duct to its normal cylindrical shape and maintains the calibre of its lumen at the site of the investigating incision.

Should there have been an *impacted* stone in the common duct the lower limb of the T tube should be sufficiently long to pass by this point in order that contraction from submucous infiltration will not occur.

Some object to the T tube because of the trauma incidental to its withdrawal. This trauma can be almost entirely avoided by excising an inverted $\vee$ from the cross arm of the T and directly opposite the long stem.



The length of time drainage of the common duct should be maintained is a moot point. It is a matter of considerable import to the patient from the viewpoint of comfort but more so from the viewpoint of complete recovery from pre-operative symptoms.

My custom is to remove the T tube in nine or ten days, provided I have been able to thoroughly dilate the ampulla by the passage of Van Buren sounds. I believe that the biliary system is drained just as effectively by the route of the patent common duct as by a fistulous opening through the skin. In fact, if there be anything in the theory that the flow of bile into the intestine is accelerated by a kind of vacuum or negative pressure produced within the duodenum by peristaltic movements of the latter, the biliary system should be better drained through the patent duct than through a tube leading externally.

Biochemical studies on my cases have revealed as prompt recovery of hepatic and pancreatic function as in those cases drained for longer periods. Moreover, the bile is not lost but is permitted to contribute normally to the processes of digestion.

Just one word about that most valuable of tests, the x-ray visualization of the gall bladder by tetraiodophenolphthalein.

1. There is no doubt but that it is irritating to the liver. Tests for hepatic function should be done before its use or postponed for three to four days after its administration.

2. In the Montreal General Hospital we put

no dependence upon abnormal findings if the substance has been administered orally.

3. It accomplishes but one thing, viz., x-ray demonstration of a normal or abnormal gall bladder or its contents. But to do this requires a comparatively normal hepatic function and a freely flowing bile stream.

If a flat plate x-ray demonstrates stone, the test is superfluous. If obstructive jaundice be present, the test is not only useless but harmful.

HEALING OF WOUNDS

Away back in 1922 I stumbled upon the fact that a mild hyperglycemia interfered with wound healing. Since that time our experience has demonstrated that hyperglycemia is responsible, more than all other causes combined, not only for delayed healing but for reduced resistance to infection.

Inasmuch as some eighty per cent of patients with biliary infection show by means of a blood sugar time curve a hyperglycemia of greater or less degree it is my custom to administer Insulin, five units every six hours, throughout postoperative convalescence. I believe this ensures a more rapid healing of the wound, a lessened incidence of mild but troublesome infection of the subcutaneous fat and an almost total absence of that most distressing accident, wound bursting.

THE OPERATIVE PROBLEM OF THE JAUNDICED PATIENT

When an obstructive jaundice has persisted for some weeks any operation is attended by the risk of continued capillary oozing because of a prolonged bleeding time. The technique of its control has been pretty thoroughly worked out.

The administration of calcium will restore normal conditions. Calcium may be given by mouth but is much more effective given intravenously as calcium chloride, five cc. of a ten per cent solution on three successive days. This solution is very cauterant and extreme care is required to prevent any leak into the subcutaneous tissues. Normal saline should be run into the vein first to establish beyond doubt that the needle is properly placed and not infiltrating about the vein. Then the calcium chloride is added, after which a goodly amount of the saline is run through to thoroughly cleanse the vein.

But here again we meet with exceptions, and the action of the calcium chloride should always be reinforced by a blood transfusion a few hours prior to the intended operation.

Recently I had in my service a woman with obstructive jaundice of only three weeks' duration who showed a bleeding time of 20 minutes. After calcium chloride on three successive days the bleeding time was still 19 minutes. A blood transfusion enabled the operation to be performed without evidence of excessive bleeding and with no postoperative capillary oozing.

It may be wise in such a patient to be content with drainage of the gall bladder for relief of jaundice and restoration of normal bleeding time before proceeding to the more extensive operation of common duct surgery. The wall of the common duct is richly supplied, or covered, by a plexus of small venules.

But this in turn brings us to a consideration of Courvoisier's law, which, like all "laws", has its exceptions which make this law all the more significant.

As you all know, Courvoisier's law is to the effect that obstructive jaundice associated with a distended gall bladder is due to obstruction of the common duct by a lesion other than stone; if due to stone the gall bladder is not distended.

In other words, a normal gall bladder is capable of distention, but a chronically inflamed gall bladder with fibrosis of its walls is not. As the usual antecedents of stone in the common duct are stone in the gall bladder with infection and chronic inflammation of that viscus the reasonableness of the law is evident.

So in cases of obstructive jaundice from stone, associated with a much prolonged bleeding time when we would wish to play safe by a preliminary drainage of the gall bladder, we may find it a shriveled-up viscus with no lumen from which to drain bile.

Now there is another operative risk in these jaundiced cases, one which has not as yet been generally recognized. I refer to the sudden relief of a long-established positive pressure in the obstructed bile ducts, extra- and intrahepatic.

Sir William deCourcy Wheeler, formerly of Dublin, now of London, in 1930 presented a paper entitled "Recoil" in which he again emphasized the evil effects of sudden relief of an abnormal positive pressure. We are all familiar with the accident of hemorrhage into the urinary bladder following emptying of that distended viscus, or of anuria because of the sudden alteration in pressure, or of edema of the lungs following the too rapid withdrawal of a massive pleural effusion.

I have had one patient with obstructive jaundice of some months' duration whose common duct I opened and drained.

On the fifth day she died in coma, deep jaundice and other signs simulating acute yellow atrophy. At autopsy the liver (which at operation was enlarged three fingerbreadths below the costal margin) was shrunken to 1240 Gm. weight and microscopically showed disintegration by rupture of the hepatic cell columns.

Just how this difficulty is to be overcome I cannot quite see.

BILE PERITONITIS

Bile leak into the peritoneal cavity is a serious matter. It produces an insidious peritonitis which is frequently fatal.

I have already referred to the advantages

of the T tube in permitting accurate closure of the incised duct.

But probably the most common cause of bile leaking into the peritoneal cavity is the non-recognition of an anomalous congenital arrangement of the extrahepatic bile passages, especially of a supernumerary right hepatic duct of small size which enters directly into the cystic duct and is divided in clearing the latter to its junction with the common hepatic duct.

I have had one such case which was recognized at the time and attempt made to drain through into the common duct. But the lumen of the anomalous duct was so small that the drainage tube was displaced on the second day. Literally quarts of bile and bile-stained exudate were aspirated from his lower peritoneal cavity and he fortunately recovered.

Another confusing anomaly is to find the cystic duct running in the wall of the common duct for a considerable distance, even down to the ampulla of Vater.

Anomalies of the cystic artery and its branches are still more common, but these are of no significance other than the annoyance because of the difficulty in seizing the bleeding point.

Benign papilloma of the common duct, rarely alone, but commonly associated with multiple papilloma of the gall bladder, may cause biliary colic from detached portions of the papilloma or may produce obstruction to the outflow of bile and jaundice.

Carcinoma of the ampulla of Vater, of the head of the pancreas, metastatic carcinoma of the lymph nodes in the gastrohepatic omentum may all produce obstructive jaundice and uncontrollable itching, for the relief of which a short circuiting operation is desirable.

This can be accomplished by a cholecystgastrostomy or duodenostomy, provided the gall bladder has a supple wall and admits bile to its lumen. For this procedure I believe a Murphy button has an advantage over suture by compressing the divided edges of the incised viscera and thus effectively controlling capillary oozing.

It is possible to ramble on into many bypaths, but time does not permit.

Dr. Fitz referred to hepatic cirrhosis and its medical treatment. I would like to say a few words of the surgical treatment of two of its complications or sequelae, viz., ascites and hematemesis.

The ascites is a transudation from the obstructed veins of the portal system. The fluid intake escapes into the peritoneal cavity. The patient is always thirsty, dehydrated and the urine output is scanty.

With the establishing of a collateral circulation between portal and systemic circulatory systems the ascites spontaneously disappears and if the liver regenerates the patient recovers, at least temporarily.

Therefore it is difficult to assess the value of such operations as omentopexy which look to the more rapid establishing of the collateral circulation.

I have latterly been using Paterson's buttons for the drainage of ascites and in three patients have had results which have not only pleased the patients but satisfied the internists who referred them.

The procedure is very simple, hence more worthy of attention.

Peter Paterson, formerly Professor of Surgery at St. Mungo's College, Glasgow, and Surgeon to the Royal Infirmary, published in the *Lancet* of October 29, 1910 a description of glass buttons which he had used in draining several cases of ascites.

The button consists of two flanges connected by a hollow stem. The technique of employment consists of their insertion so that one flange is within the peritoneal cavity, the other between the layers of the anterior abdominal wall. To prevent blocking of the aperture by adherent omentum, Paterson amputated the necessary portion of that structure.

He publishes no statistics but states he "has performed this operation in several cases of ascites secondary to malignant disease and also in cases of cirrhosis of the liver, with marked diminution of the abdominal distention, and to the great relief of the patients".

Thomas Tannahill, Glasgow, reported a case in the *Brit. M. J.* February 15, 1930, in which he has revived the use of Paterson's buttons, in a patient with hepatic cirrhosis with marked ascites who was afforded great relief. He modified Paterson's procedure by doing omentopexy into the upper portion of the wound, instead of amputating the omentum.

Following Tannahill's technique I have employed the Paterson buttons in three patients with troublesome ascites from hepatic cirrhosis.

In all three there were immediately noted

1. Relief of thirst.
2. Increase of urinary output.
3. Improvement in strength, color and nutrition.

The procedure is not advanced as a cure for hepatic cirrhosis. It simply offers an alternative to the otherwise necessarily frequent paracentesis of the abdomen, and returns to the patient's tissues the fluid which is otherwise lost, and gains valuable time for the spontaneous establishment of a collateral venous circulation and a possible regeneration of the liver.

HEMATEMESIS

The relief of portal venous obstruction is brought about by the establishing of a collateral circulation between the portal and systemic venous systems.

The easily demonstrable sites of gross communication are

1. Lower end of esophagus, esophageal varix.
2. Lower end of anal canal, hemorrhoids.
3. Umbilicus, Caput medusae.

Less gross, but quite effective, communications are noted in the dilated veins of the abdominal wall, some proceeding upwards toward the axillae and others proceeding downwards toward the groins. Others just as effective but not demonstrable during life are situated in the retroperitoneal tissues posteriorly.

These compensating varicosities may give rise to troublesome or even dangerous manifestations.

Hemorrhage from esophageal varices may be not only alarming but may even threaten life. Esophageal varices are not necessarily indicative of portal obstruction. They may and do frequently exist in association with any form of splenomegaly. The enlarged spleen demands an increased blood supply and for the return of that increased blood flow there must be a compensating dilatation of the veins in the neighborhood, including the veins of the lower esophagus.

As somewhat of a digression, permit me to spend a few moments in consideration of the treatment of violent hematemesis.

With the patient in collapse because of the large amount of blood loss it is not permissible to make a routine examination, and therefore it is at times impossible definitely to diagnose the nature of the lesion giving rise to the bleeding.

Moreover, although an individual may survive a tremendous initial blood loss, a repeated and much smaller bleeding will result in death. Therefore active resuscitation methods must be avoided.

In other words, the treatment indicated is to maintain the patient just alive and no more.

It is necessary to attempt to visualize the lesion which may be present.

Over 80 per cent of hematemesis results from a chronic peptic ulcer.

But severe bleeding may arise from an acute gastric ulcer, from septic or aseptic thrombosis of the stomach veins, from follicular gastritis or duodenitis, from diverticulum of the duodenum, or from benign or malignant tumor of the stomach.

It may also arise from varices in the stomach wall or esophagus because of portal obstruction, or in any form of splenomegaly. Again it may be due to blood dyscrasias as in the purpuras, primary anemias and leukemias.

With such a varied etiology it is apparent that treatment can be based only upon the symptom of bleeding and the acute anemia arising therefrom, with every precaution to avoid prompt resuscitation and elevation of blood pressure, with blowing out of a soft ill-formed clot and renewal of bleeding.

Routine treatment should be as follows:

1. Elevate the foot of the bed (14 inches). Small pillow beneath head, not under shoulders.
2. Morphia in small repeated doses to restrain restlessness.
3. Nothing by mouth, not even cracked ice. Rinsing and swabbing permissible.
4. No stimulation either by drugs or fluid, unless death be imminent as indicated by falling blood pressure, air hunger, etc.
5. Increase coagulability of blood by injection of hemostatic serum or small blood transfusion (200 cc. or less).
6. Measure urinary output as a guide to the administration of fluid by hypodermoclysis (axillary areolar space, submammary space), rarely by rectum, and still more rarely by intravenous route.
7. Absolutely no physical or other examination until the threat of death from recurring hemorrhage has passed; blood pressure estimation excepted.

Under the above plan of treatment all *venous* bleeding will cease. All bleeding from *superficial* ulcers will cease, and recurring hemorrhage indicates that the source of the bleeding is from a chronic penetrating peptic ulcer with, in all probability, a flute-hole opening in an arterial vessel.

Such a lesion will not permanently cease bleeding except by surgical control, and desperate measures must be taken.

DISCUSSION

DR. FRANK H. LAHEY, Boston: One does not come into any disagreement when he listens to men who have had sufficient experience by which to establish their positions and who are of sound judgment. There isn't a single thing which has been said with which I would personally be in disagreement.

It would be wrong, I think, if I did not say something, based upon our own experience, in relation to some of the facts which have come up in connection with these papers, because after all, our value to you is related to our experiences with these problems, to our errors and the attempts to correct them.

As to coagulation and bleeding time, our experiences with these is that they have very little value. We have felt that coagulation time and likewise the administration of calcium have very little value as prognosticating or as a protection against the possibility of hemorrhage at the time of operation. It is characteristic of the bleeding time in jaundiced patients treated with calcium to see sudden drops in this bleeding time together with sudden rises within a very short period of time, and we have not been impressed with the fact that calcium protects these individuals against the possibility of hemorrhage. The suggestion made by Dr. Hinton of the Massachusetts General Hospital of using the sedimentation rate is open also to a considerable degree of error, but it has proved of greater value in

our hands in prophesying the value in hemorrhage than has coagulation time and bleeding time.

We have come to depend almost entirely upon the administration of large amounts of fluids and glucose intravenously, and of whole blood transfusion as a protection against the possibility of hemorrhage in jaundiced patients. In spite of all this, plus the addition of calcium, some of these patients still will bleed. I know of no rule at present to determine with certainty which one will bleed and which one will not bleed.

I think if there is one thing that we have learned, and if I had charge of a hospital I would make it a rule, and that is that the plan of sending patients into a hospital one night and operating for serious lesions the next morning should cease. There has been many a patient who has lost his life on the basis of this plan of doing surgery. Surgery is too serious a problem to be approached that hastily. It gives an opportunity, if the patient is held over one day at least, to deliberately estimate the risk and to prepare the patient. This is doubly true in the jaundiced cases and in the gall stone cases.

We have had it impressed upon us with the thyroid cases, also. Think how we learned it with prostates. Think of the number of people who have perished because in the past we did not know about the need of preparation. The same thing is very true of the biliary tract cases. Many a patient with and without jaundice and gall stones has died because of the lack of adequate preoperative preparation. Therefore, we keep the patients in bed preoperatively for several days. I think there is nothing that is more valuable than the preparation with fluids, glucose and a high carbohydrate diet. We know, too, how well the liver tolerates all degrees of insult, but if you can raise the reserve of the liver by glucose, fluids, and a high carbohydrate diet, it distinctly lessens the risk.

Anesthesia plays a considerable part also. The worst anesthesia for the liver is chloroform; the next is ether; the next nitrous oxid and ethylene and least injurious is local or spinal anesthesia.

Cholecystography is, of course, a great addition to our diagnostic resources, but I think one should realize that these laboratory measures must not replace clinical evidence. We say that when a patient has a clinical history of typical gall stone colic, even though the gall-bladder fills and empties with the dye, that we will operate on him, and if the patient has no abnormal history and his gall-bladder does not fill or empty, we will not operate on him. In other words, we will not fail to operate because of x-ray evidence, and we will not operate solely because of x-ray evidence unless the clinical features go with it.

Not in many cases, but in a few cases, we have seen the gall-bladder empty and fill in the presence of stones demonstrated at operation. Our experience with the non-filling gall-bladders will be of interest to you.

In the presence of acute duodenal ulcer, the gall-bladder tends not to fill with cholecystography as well as in pregnancy; and in the presence of high degrees of colitis, it tends not to fill.

When patients have simple, non-filling of the gall-bladder we send them home and try to have them come back a few weeks later and repeat the test. Then, in many of the cases the gall-bladders will fill.

I have enjoyed very much listening to the two sound and excellent discussions of the subject.

DR. GEORGE HOLMES: Dr. Bazin has raised a point that I would like to say a word about. He stated that the examination with the dye was useless if stones were demonstrated. As a general rule, that is so. But there are certain cases when it may be of value. In some cases it is important to demonstrate the flexibility of the walls of the gall-bladder.

If you want to find out whether the gall-bladder is flexible, even though stones are present, the dye test may give you that information.

Then, with respect to the question of examination in the presence of jaundice, I wouldn't like to inject the dye into the circulation in these cases. But I am quite sure that it is comparatively harmless when given orally, and that it may help to distinguish the type of jaundice. There is a small group of cases where the diagnosis is in doubt, which are eventually found to be carcinoma of the pancreas, and a non-filling of the gall-bladder may be one of the earlier signs. It may appear even before jaundice. Of course, it does appear in the case of jaundice. I agree with Dr. Lahey in regard to the value of the test. What he says is true of all laboratory examinations, the x-ray examination is a laboratory method, although roentgenologists dislike to admit it. Whether the patient is operated upon depends upon clinical findings and not upon laboratory findings.

MISCELLANY

COUNTY MEDICAL SOCIETY DISCUSSES MEDICAL RELIEF FOR PERSONS RECEIVING PUBLIC AID

The question of medical relief for persons receiving public aid was the principal topic of discussion at the 29th annual meeting of the Hillsborough County Medical Society at the County Hospital Tuesday, November 14.

There have been some differences between the newly created state relief administration and some of the doctors relative to the handling of medical cases and the purpose of the discussion is to clarify the situation and iron out all the difficulties.

Dr. R. J. Graves and Dr. D. E. Sullivan, both of Concord, president and secretary respectively of the New Hampshire Medical Society, attended the meeting and led this discussion which was entitled, "Medical Relief of the Indigent."

Miss Eunice E. Patch, director of the state relief administration, was expected to attend the meeting, but she was unable to come.

Dr. T. F. Rock of Nashua was elected president of the society at the business session in the morning. Dr. Z. A. Lavoie was named vice president and Dr. Deering G. Smith of Nashua was reëlected secretary-treasurer. Dr. H. M. Morse of Peterborough was elected censor for three years and Doctors J. S. Larochelle of Manchester, R. J. Joyce of Nashua and B. A. Pease of Greenville were elected delegates to the state conventions for two years.

Two papers were read during the afternoon. Dr. George C. Wilkins of this city read one on "Cancer Clinics and the Importance of the Early Diagnosis of Early Cancer," and Dr. R. H. Smithwick of Boston read a paper on "Peripheral Vascular Diseases."
—*The Union, Manchester, New Hampshire.*

THE USE OF BENZYL-METHYL-CARBINAMINE-CARBONATE IN THE TREATMENT OF RHINITIS*

BY HARRY V. BYRNE, M.D.‡

A NEW drug for the symptomatic treatment of rhinitis has recently been developed. This preparation is a volatile carbonate of benzyl-methyl-carbinamine†. The compound is related structurally to both ephedrin and epinephrin with somewhat similar pharmacological and physiological properties. Hartung and Munch[1], and Piness et al[2] report a marked rise in the blood pressure following the administration of the drug. The latter investigators state that they found coincident to the rise in blood pressure a suppression of the secretions of the mouth and nose. The reported observation of Piness and his coworkers of the prolonged effect of benzyl-methyl-carbinamine and the minimizing of the secretion of the nasal and aural cavities led to the use of the drug in a number of patients suffering from some of the many forms of rhinitis.

The ease of administration of the drug, by inhalation rather than by spray or jelly, presented some advantages. In addition it was desired to find some drug having the effect of shrinking the nasal mucosa without occasioning a thickening and dryness often observed following prolonged treatment with ephedrin. This question becomes of great importance when one remembers that the patient, himself, uses ephedrin for any and all types of nasal disorders without consulting the physician.

In the treatment of vasomotor rhinitis, where the disease per se is of short duration and self-limited, treatment at best is only palliative and to be of any value, must be prompt in effect and lasting in action. Protein therapy has yielded only about 60 per cent cures, despite careful sensitizing tests to determine the protein causing the condition, and usually it has to be repeated each year prior to and during the pollenization period. The purpose of this study was not to find a cure for acute and vasomotor rhinitis, but only to note any improvement in palliating the disease by using a new preparation in an old way. Just what rôle allergy and to what extent infection played a part were not germane to this investigation.

EXPERIMENTAL

A study of 51 consecutive patients suffering from various types of nasal and sinus infection was made during the months of August to November, 1931 in the Aural Outpatient Department of the Boston City Hospital. These patients were not selected in any way and in certain of the cases, the controls used were patients with similar conditions treated with ephedrin (Lilly) in some one of its various forms.

I. Vasomotor Rhinitis (Hay Fever)

Of the number of patients treated 26 or 51.9 per cent were patients suffering with acute vasomotor rhinitis. They all gave histories of previous attacks, the earliest being the initial attack, and the oldest dating back six years. Seven of these patients, or 27.9 per cent, had received previous sensitivity tests and injections for foreign protein therapy. They all presented the usual signs associated with their condition, namely, pale engorged nasal mucous membrane with excessive nasal discharge of a thin watery secretion, with sneezing, and conjunctivitis to a marked degree. A deviated septum, impinging in four cases, on the middle turbinate, was demonstrated in nine of these cases. In most cases, showing a deviation of either cartilaginous or bony part of the septum, submucous resection of the septum was done before any medication was attempted.

Eighteen or 69 per cent of the patients in this group showed prompt and striking improvement following inhalation of the drug, and were relieved almost at once of the subjective symptoms of sneezing and itching of the eyes and nose. To illustrate this point the following two cases were taken as examples:

CASE 1. W. F. G., aged 34, married, white accountant. Patient has had attacks of sneezing, lacrimation, conjunctivitis, and watery nasal discharge for the past six years which generally appeared about August 15th and September 20th. He was tested with proteins and found to be sensitive to the pollens of goldenrod and ragweed. For two successive years he received preseasonal and seasonal injections which partly relieved him of his symptoms throughout the period of the disease. One year ago he used ephedrin spray and was relieved. When seen at the clinic on August 29, 1931, he had been sneezing and had had the other symptoms of his condition for one week, and at the time of the examination was suffering from a paroxysm of sneezing. Examination of his nose showed a badly deviated septum toward the left, in its anterior part. The mucous membrane was pale, watery, and congested. The inferior turbinates on both sides were swollen and pendulous with watery fluid in the floor of the nose. Transillumination of the sinuses was clear. Subsequent x-ray examination also showed no sinus involvement. Because of the intensity of the attack, benzyl-methyl-carbinamine-carbonate was used at once; the sneezing stopped immediately. Half an hour later, after the patient had cleared his nose, the mucous membranes were found to be dry, but still slightly engorged. Lacrimation had ceased,

*From the Aural Department of the Boston City Hospital.

†The benzyl-methyl-carbinamine-carbonate used in this investigation, manufactured under the name "Benzedrine Inhaler," was obtained from the Smith, Kline & French Laboratories, Philadelphia.

‡Byrne — Assistant Surgeon in Ophthalmology, Boston City Hospital 1933-. For record and address of author see "This Week's Issue," page 1070.

although conjunctivitis was still present. The patient was seen daily for three more visits, and, when using the drug, had no further symptoms. One month later he was still free from trouble, although by that time, of course, the disease had run its usual course.

CASE 2. M. McG., 25, single, white stenographer. Patient had vasomotor rhinitis of two years' duration. The septum showed no pathology. The inferior turbinates were engorged, and a watery fluid was present in the floor of the nose. The mucous membrane was pale and boggy. Tonsils and adenoids had been removed in childhood. Examination of the sinuses by transillumination was negative. The patient had never been sensitized and was subject to attacks every August and September. She had used ephedrin in spray and jelly forms for two years. The attacks during this time were severe enough to keep her home from work. The patient obtained marked relief from benzyl-methyl-carbinamine-carbonate. Her nasal secretions dried up in 24 hours. There was gradual shrinkage of the mucous membranes in 48 hours. Sneezing ceased after two inhalations, while conjunctivitis was relieved in 24 hours.

The most characteristic improvement of the cases suffering from vasomotor rhinitis was seen in those patients who came to the clinic early in their seasonal attack. The relief afforded them was noted clinically, first, in the cessation of the sneezing attack, followed by a diminution in the amount of lacrimation and intense conjunctivitis. Intranasal examinations usually showed a dry nasal mucous membrane with decongestion of the turbinates, within 48 hours, in practically all cases. The anemic appearance of the membrane was much slower in regaining its normal color, even after one to two weeks' steady use of the drug.

The remaining eight cases, 31 per cent, did not show any prompt improvement other than a lowered intensity of their symptoms, particularly sneezing. In these cases the stuffiness of the nose and the nasal discharge, with its attendant feeling of fullness, persisted despite the use of the drug. In five of these cases, these symptoms were relieved by the extensive institution of nasal sprays of ephedrin, coupled with tamponage of cocaine and adrenalin in the clinic.

II. Acute Rhinitis

Only ten cases, or 19.6 per cent of the patients studied in this investigation, fell into this group. This was probably due to the relative unimportance of the disease from the layman's viewpoint and the facilities of home treatment. Such patients, as did present themselves, had some underlying pathology from which they really sought relief. It should be pointed out here, and will be emphasized still more later, that patients suffering from ordinary head colds, whether of the acute or chronic type, rarely appeared in the Outpatient Department for this reason alone. Consequently, the cross section of our patients was not entirely analogous to those found in private practice, there being a far greater incidence of underlying pathology. Septal deviations were present in three of these cases, and diseased tonsils and adenoids in the remaining seven cases. In every case the necessary surgery was advised, and the inadequacy of medical treatment in the presence of such foci discussed with the patient.

Inhalation of the drug relieved the feeling of fullness and itching in the nares of all patients, but had a less pronounced effect than was found in patients suffering from vasomotor rhinitis. There was, however, some permanent decongestive action of the drug noted on the turbinates, and practically every patient experienced better breathing facilities almost immediately following the use of the drug. The amount of the watery discharge, with its subsequent irritative action on the external nares, was decreased and diminution of the conjunctivitis present was noted.

CASE 3. H. F., aged 24, single white nurse, came to the clinic suffering from a severe head cold. Examination of the nose revealed marked redness and congestion of the mucosa over the septum and inferior turbinates. Breathing was difficult due to the obstruction, and there was a steady nasal discharge of a thin watery secretion. Lacrimation was present to a marked degree. The pharynx was coated with the same type of secretion as the nasal discharge. Both tonsils were hypertrophied and cryptic with moderate injection of the pillars. She gave a history of frequent head colds and sore throats, especially in winter and spring.

Benzyl-methyl-carbinamine-carbonate was used with marked diminution of the nasal discharge. She found considerable relief from the nasal obstruction and examination of the nose on the following day showed definite improvement of her condition, as indicated by the decreased congestion of the turbinates. Three days' treatment of the upper respiratory condition relieved her of the acute attack, and tonsillectomy was later performed to prevent recurrences.

III. Chronic Hypertrophic Rhinitis

Although it was felt that, in patients suffering from both hypertrophic rhinitis and chronic catarrhal sinusitis, it was very unlikely that any beneficial results would be obtained from the use of the drug, a few were treated and certain matters of interest appeared that warrant their inclusion in this report. The six cases, 11.6 per cent of the entire group comprising this study which came under our observation, had a history of symptoms ranging from several months to ten years. Various forms of treatment had been given, including the usual adrenalin or ephedrin sprays and nasal tampons. Transillumination and x-ray examination revealed no involvement of the sinuses in these cases. The patients did show, however, an enlarged inferior or middle turbinate. The same type of fibrotic mucous membrane was present throughout the nares and on the septum, but no polypi were present in the nose.

The use of the drug in these cases was uni-

formly unsuccessful. There was no evidence of any change in the appearance or character of the nasal mucosa. Practically all patients of this type, in whom the drug could be used, noticed a diminution in the amount and rate of nasal discharge with better breathing facilities. It was felt, however, that cases of the above type could be offered little help until the existing surgical condition was remedied. The following two cases are illustrative of this point.

CASE 4. M. C., aged 65, single white woman, retired, gave a history of "nose trouble" for six or seven years, which was characterized by a nasal discharge, requiring three to four handkerchiefs, and an irritative postnasal discharge, most noticeable in the morning. Examination of her nose showed early atrophic changes in the mucosa overlying the turbinates with adequate airway and a normal septum. The mucosa of the nose was a dull reddish grey color with loss of the normal erectile epithelium over the inferior turbinate, and an apparent increase in the mucous-bearing epithelium of the middle turbinate. Free discharge of a glistening type was present in the floor of the nose. No polypoid degeneration was present, nor were any crusts or odor noticeable. The pharynx was dry and dull in appearance with a similar postnasal discharge present.

Palpation of the turbinates with a probe showed a lack of resiliency to the mucosa which remained pitted under pressure longer than normal.

Benzyl-methyl-carbinamine-carbonate was used rigorously for a week in an effort to check the nasal discharge. There was no noticeable change in the appearance of the turbinates, nor did the discharge cease. In this case it was felt that the blood supply to the turbinates had been altered for so long that any further constriction of the capillaries in the mucosa might aggravate the condition already present.

This patient eventually was treated by electrocoagulation in an effort to lessen the nasal discharge.

CASE 5. D. F. G., aged 34, white, married, salesman, was seen at the clinic three days after the onset of a severe head cold. His chief complaint was pain in the right eye and difficulty in breathing. Examination revealed a septum markedly deviated, in the cartilaginous as well as the bony portion, toward the right and compressing both the inferior and middle turbinates on that side. The mucosa overlying the turbinates and septum was inflamed and congested with almost complete obliteration of the airway. Swelling of the right lower lid and marked lacrimation and conjunctivitis were present. Excoriated areas in the right vestibule and on the lower lip were present from irritating nasal discharge. Attempts to effect decongestion of the mucous membrane by inhalation of benzyl-methyl-carbinamine-carbonate were unsuccessful, due largely, perhaps, to the inability of the nostril to properly admit the inhaler. Even after shrinkage with tampons of cocaine and adrenalin, the mechanical obstruction of the septum would not permit easy inhalation of the drug and further use of it was discontinued. Ephedrin spray was then tried. No medication, however, applied by inhalation or spray seemed to afford much, if any, relief in this particular case, since the condition was one of structural displacement of the normal anatomy of the nose. Submucous resection of the septum was logically the procedure of choice, and the patient was accordingly advised of the inadequacy of any medical treatment.

IV. Chronic Catarrhal Sinusitis

Nine patients, 17.6 per cent of the group studied, had had a chronic nasal discharge of thick tenacious secretion accompanied by irritating postnasal discharge of the same type. The mucous membrane was of a dull, brownish red color with pendulous, boggy, inferior turbinates. On palpation with the probe, the mucosa was found to be thickened and fibrotic. The pathology in three cases was ethmoiditis; of the others, four showed maxillary sinusitis, with a thickening of the mucosa, and two, frontal sinusitis. In none of the latter was frank pus demonstrable by x-ray. In one case of ethmoiditis and two cases of frontal sinusitis, the use of the drug, benzyl-methyl-carbinamine-carbonate was followed by a dull frontal headache and a sense of internal pressure with a feeling of dryness and stuffiness of the nose and nasal pharynx. The voice assumed a nasal tone and in one case nausea ensued. Application of tampons saturated with ten per cent cocaine and adrenalin relieved these patients from the untoward effect of the drug and left them with no permanent discomfort. In these three cases, the headache, following within 30 minutes the administration of the drug, had persisted for six to eight hours afterwards. Examination of the nose in these patients showed a dry glistening mucous membrane with turgescence of the inferior and middle turbinates. There was no free secretion in the middle meatus or floor of the nose, and it was felt that the headache was caused by mechanical obstruction of the nasofrontal duct of the frontal sinus or the anterior ethmoidal cells in the case of ethmoiditis, giving rise to a so-called "vacuum type" of headache.

It cannot be concluded from this limited experience with patients suffering from sinusitis that the drug has no beneficial effects in this condition, but in the presence of definite pathology giving rise to such a condition, the indiscriminate use of a drug whose chief action is that of constriction is to be avoided.

DISCUSSION

In general, experience with this drug shows it to be a useful adjunct in the treatment of certain types of rhinitis, particularly hay fever and acute rhinitis. In all cases where the nasal discharge is of a thin watery type and seems to be due to transient changes in the osmotic tension of the capillaries of the mucosa, inhalations of the drug, working chiefly through vasomotor control, can inhibit the amount of secretion. The duration of the effect of the drug seems to be about four to five hours. One of the patients (Case 2) found that inhalations about three times in 24 hours were sufficient to keep the air passages free and the secretion limited. Case 1

required inhalations at three hourly intervals to be free of the sneezing and discharge. Other cases observed improvement by using the drug only twice a day, while those patients in whom no relief was obtained found that hourly inhalations did not suffice. In general, it was noted that the more severe cases required more frequent inhalations and the milder ones less. Tentatively, each patient on his or her first visit to the clinic was advised to use the drug about three or four times a day and, on the second visit, the time element was altered, if necessary. By its constrictor action on the blood vessels, the turgescence of the mucous membrane was diminished and prompt improvement in breathing noted. The drug was most useful in cases of rhinitis of a non-purulent nature, since it is in those cases that its constricting action is most effective. Purulent nasal discharge is, in itself, evidence of underlying pathology and here the drug is of little value. It would seem, therefore, that choice of the drug limits itself to acute and vasomotor rhinitis and that from it one can obtain considerable benefit in palliating the distressing symptoms, with noticeable benefit to the mental and physical condition of the patient.

It must also be pointed out that this drug is an active pharmaceutical substance. Overdosage has been followed by symptoms resembling the effects produced by cocaine. It is advisable, therefore, that in the use of the material the same specific directions be given, as would be employed for any other active preparation.

SUMMARY

1. Fifty-one cases of rhinitis were treated with benzyl-methyl-carbinamine-carbonate in the Aural Clinic of the Boston City Hospital.

2. The results obtained in the treatment of vasomotor rhinitis (Hay Fever), and acute rhinitis were definitely encouraging.

3. There was definite proof, in this type of case, that the amount of secretion was diminished, the subjective itching and feeling of fullness relieved, and decongestion of the mucous membrane accomplished.

4. The results obtained by using the drug in those cases of sinusitis presenting themselves for treatment were poor and, in certain of cases, increased, rather than diminished, the severity of the symptoms.

5. It is felt that the drug should be used after a careful examination of the nose has been made by a competent rhinologist and the character and cause of the rhinitis determined. The drug should be prescribed with careful directions.

6. The ease of the administration of the drug recommends itself to the ambulatory patient and tends to make more certain the patient's use of the material.

NOTE: Since the writing of this article Benzyl-methyl-carbinamine-carbonate, manufactured by the Smith, Kline & French Laboratories, has recently been accepted for New and Non-Official Remedies by the American Medical Association under the name "Benzedrine Inhaler."

REFERENCES

1 Hartung, Walter H., and Munch, James C.: Amino alcohols. VI. The preparation and pharmacodynamic activity of four isomeric phenylpropylamines. J. Am. Chem. Soc. 53:1875, 1931.

2 Piness, George; Miller, Hyman, and Alles, Gordon A.: Clinical observations on phenylaminoethanol sulphate. J. A. M. A. 94:790, 1930. Read before the Section on Pharmacology and Therapeutics at the Eighth Annual Session of the American Medical Association, Portland, Ore., July 12, 1929.

AGRANULOCYTOSIS

BY GREENE FITZ HUGH, M.D.*

AGRANULOCYTOSIS is a disease characterized by sudden onset, fever, in most cases sepsis of greater or less degree (usually oral sepsis), and extreme leucopenia with a marked reduction in the percentage of polymorphonuclear cells. The mortality is high (80 per cent or more). It is called agranulocytic angina (because of the extreme oral and tonsillar sepsis that is present in most cases); idiopathic neutropenia; malignant neutropenia and granulocytopenia.

The first description of the disease was given in 1907 by Turk[1] who reported a case that showed almost all lymphocytes in the smear and terminated fatally in four days. In 1922, Schultz[2] proposed the name agranulocytic angina for a group of cases with gangrenous stomatitis and a remarkable blood picture, occurring in middle-aged women, usually fatal. Since 1922 case reports have appeared from time to time, at first infrequently, in the last five years quite commonly. In some reported cases which were followed closely[3, 4] the fall in white blood cell count and the marked decrease in the percentage of polymorphonuclear cells have preceded the other symptoms of the disease, including the sepsis, oral or elsewhere, and may be considered to be the fundamental disorder. In others the change in the blood picture is secondary to sepsis.

The clinical picture of agranulocytosis is described by Ordway and Gorham[5] based on an analysis of 82 cases. The onset is abrupt with high fever (101-105° F.) and malaise. There is almost always some inflammatory change in the oral cavity, and ulceration and necrosis with membrane formation are frequent. There is usually little tissue reaction about the ulceration or necrosis, and since this is not ordinarily the case in oral sepsis it should suggest the

*FitzHugh — Assistant in Medicine, Massachusetts General Hospital. For record and address of author see "This Week's Issue," page 1070.

presence of agranulocytosis. The oral or other sepsis may not be present from the onset of the disease. There may be chills, headache, vomiting and general muscle pains. The regional lymph nodes are swollen and tender in about half the cases. The liver and spleen may or may not be enlarged. Jaundice and petechial hemorrhages into the skin and viscera occur at times. (In Jackson's cases, jaundice and petechial hemorrhages have been infrequent[6]. They are common findings in the terminal stages of aleukemic leukemia with which agranulocytic angina is easily confused.) The platelets are usually normal in number. The diagnosis is established by the low white blood count, commonly 1500 or less (the average in Ordway and Gorham's series of 82 cases is 1210) with a preponderance of lymphocytes. Eosinophils and basophils are usually not present. In the case reported below no eosinophils had been found in blood smears up to five months after recovery except on one occasion, 71 days after the onset, when one eosinophil was found in counting 100 cells.

Before 1930 the treatment of agranulocytosis was largely supportive, since no known procedures influenced its course. Transfusions were used in the hope of supplying white blood cells until the marrow began to function normally. Good results have been reported from small doses of x-ray. Since both of these procedures may produce a fall in the white blood count, they should not be used. Recent work indicates that the use of nucleotide definitely lowers the mortality in agranulocytosis.

Some of the work preceding the clinical application of nucleotide is so interesting that it is briefly outlined from 1887 up to the present time. In 1887, Altmann[7] isolated nucleic acid. In 1891, Horbaczewski[8] correlated digestion leucocytosis with increased uric acid in the blood. In 1892, Metchnikoff[9] emphasized the phagocytic power of polymorphonuclear leucocytes as a means of destroying bacteria. In 1893, Vaughan[10] advocated the use of nuclein, on theoretical grounds, to increase the germicidal power of the blood. In 1897, Ames and Huntley[11] studied the apparent production of leucocytosis by nucleic acid. They found an increase in the leucocyte count and an increase in the production of young cells. They felt that the presence of young cells proved that the response was due to a direct effect of nucleic acid on the marrow, causing an increased delivery of cells from the marrow. Their work was valuable, but practical application of the findings to the disease in man was not attained until Jackson[12] began to use nucleotide in the treatment of agranulocytosis in 1930. In 1899, Milroy and Malcolm[13], using the sodium salt of yeast and thymus nucleic acid and their decomposition products, thymic acid, adenine, guanine and cystosine, found, after subcutaneous injections in rabbits, an increase in the white blood count from 5500 to 6800 and from 6000 to 7500. From 1912 to 1926, various authors suggested the use of nucleic acid derivatives in various diseases, including pneumonia. In 1923, Habetin[14] suggested the injection of 10 cc. of a five per cent solution of sodium nucleinate as a bone marrow test, describing the reaction in healthy individuals as an increase of from 40 per cent to 60 per cent of white blood cells. In 1924 Jackson[15] demonstrated the presence of pentose nucleotides in normal human blood. In 1926, Larsell[16] studied the hematopoietic effect in rabbits of cells, nuclei and nucleic acids from fowls' blood. In 1927 Doan et al[17] produced a leucocytosis in rabbits with sodium nucleonate, adenine and guanine. They pointed out that, although these chemicals contain substances calling forth neutrophils so long as there is a reserve of them in the bone marrow, they lack any factors that will maintain the level of reserve cells in the marrow. This fact is probably equally true in nucleotide therapy in man. In 1930, Reznikoff[18] reported the effect of adenine and guanine in agranulocytosis and, in 1931, Jackson[12] reported a series showing a distinct lowering of mortality by the use of nucleotide (K96).*

The following case is presented because it shows the important clinical features of the disease and the use of nucleotide (K96) seems to have brought about recovery.

The patient, a woman 62 years of age, began to complain of a mild sore throat December 31, 1931. Her temperature varied from 98 to 99.6 up to January 4. The throat symptoms were mild and the patient felt fairly well until January 6, when she developed rather marked prostration. The tonsillar gland on the left became swollen, and several small areas of ulceration with only little tissue reaction appeared on the roof of her mouth. The tip of the nose, the right ear and the anus showed evidence of mild infection. The white blood count was found to be 1000 with 98 per cent lymphocytes in the smear.

Nucleotide (K96), 0.7 gram, was given intramuscularly twice a day for four days beginning January 8 and once a day thereafter until January 22. On January 9 there was a severe chill and the patient became desperately ill. From then until January 14, her temperature varied from 102 to 104°F., her pulse from 90 to 100 and her respirations from 25 to 30. On January 11, slight jaundice appeared and lasted four days. On January 14, seven days after treatment was begun, there was definite clinical improvement, coincident with the reappearance of polymorphonuclear cells (24 per cent) in the blood for the first time since January 6.

Jackson[12] has pointed out that improvement generally occurs clinically and hematologically on about the fifth day of nucleotide therapy and the majority of his cases that recovered began to improve clinically on the third or fourth day. In this case clinical and hematological improvement did not occur until the seventh day. On that day, the white blood count, which had fallen to 200 cells on the sixth day, was 400. The increase in the number of white blood cells to a normal level was also delayed beyond the usual time. It had increased to only 2900 18 days after nucleotide therapy was begun. It seems probable that the delayed increase in the total white blood cell count was due to the intercurrent infection which developed. The amount of nucleotide used may have been a factor. Re-

*Now called Pentnucleotide (Smith, Kline & French Co.).

cently Jackson[19] (Case II) has noted an apparent relationship between nucleotide dosage and rapidity of response. In the majority of Jackson's cases[12], the total and differential count was normal 10 days, not infrequently eight days, after treatment was started. This patient's differential count was normal nine days after treatment started.

The sepsis which occurred was located in the parotid glands, nose, right ear, neck, right groin, anus, left thigh and left ankle. In the left ankle, it did not appear until three days after the patient had begun to improve. In the left thigh, it appeared three days later and, in the parotid glands, the following day. This delay was probably due to the fact that the absence of polymorphonuclear cells allowed bacterial growth which resulted in no cellular response until there were enough of these cells present to infiltrate the involved areas. Jackson[19] and Ordway and Gorham[5] have noted a similar correlation between the sepsis and the leucocyte count in some cases. It was necessary to open and drain at various times the glands on both sides of the neck and in the right groin and the abscesses of the left ankle and the left thigh. Cultures from all these areas grew pure cultures of Staphylococcus albus. The fact that this mild organism was the invader may explain the absence of a general septicemia in this case.

On March 6, the patient was allowed up and, on March 12, 65 days after the onset of the disease, she was able to walk. She has been in good health since with a leucocyte count ranging from 4250 to 7250. No eosinophils were found in smears up to five months after recovery except on March 13 when one eosinophil was seen in counting 100 cells. There were present in a smear in March, 1930 at a routine examination, 60 polymorphonuclears, 34 lymphocytes, two eosinophils and four basophils. Her white blood counts are given in Table I. The differential counts showed 96 per cent lymphocytes the first four days after treatment was started. Polymorphonuclear cells appeared (24 per cent) on the seventh day. Immature cells were present in smears up to 29 days after treatment was started.

TABLE I

	WBC		WBC
Jan. 7	1000	Feb. 2	5600
" 8	600	" 6	7700
" 9	750	" 29	5650
" 10	250	Mar. 4	5150
" 11	200	" 13	5550
" 12	350	May 3	5750
" 13	200	June 11	5550
" 14	400	" 26	7250
" 15	1000		
" 16	900		
" 17	1050		
" 18	1000		
" 19	1700		
" 20	2000		
" 21	2350		
" 25	2900		
" 30	3400		

SUMMARY

The points of interest in this case are (1) the fact that nucleotide therapy appears to have brought about recovery, (2) clinical improvement did not occur until the seventh day of treatment, whereas, in the majority of the cases in Jackson's series that recovered, clinical improvement began on the third or fourth day, (3) the total white blood count did not approach a normal level until 18 days after treatment was started, in contrast to Jackson's cases where the change usually occurred between the eighth and tenth days. It seems probable that the delayed response was due to intercurrent infection in this case.

It is possible that further investigation will show that larger or more frequent doses of nucleotide are required in cases similar to this one. Until more work has been done, it is important to use the dosage recommended by Jackson.

REFERENCES

1 Turk, W.: Septische Erkrankungen bei Verkümmerung des Granulozytensystems. Wein. klin. Wchnschr. 20: 157, 1907.

2 Schultz, Werner: Ueber eigenartige Halserkrankugen. (a) Monozytenangina. (b) Gangräneizierende Prozesse und Defekt des Granulozytensystems. Deutsche med. Wchnschr. 48: 1495 (Nov. 3) 1922.

3 Roberts, S. R., and Kracke, R. R.: Agranulocytosis. J. A. M. A. 95: 780, 1930.

4 Rutledge, R. H., Hansen-Pruss, O. C., and Thayer, W. S.: Recurrent Agranulocytosis. Bull. Johns Hopkins Hospital. 46: 369 (June) 1930.

5 Ordway, T., and Gorham, L. W.: Agranulocytic Angina. Oxford Monographs on Diagnosis and Treatment. New York, Oxford University Press. 9: 204, 1930.

6 Jackson, Henry Jr.: Personal Communication.

7 Altmann, R.: Ueber Nucleïnsäuren. Arch. f. Anat. u. Physiol. (Physiol. Abst.) 1889, p. 524.

8 Horbaczewski, J.: Die Ausscheidung der Harnsäure und die Zahl der Leukocyten im menschlichen Blute nach Aufnahme von Chinin, Atropin, Pilocarpin, Antipyrin und Antifebrin. Sitzungsber der k. k. Wiener. Akad. der Wissensch. C, part 3, reference B:101, 1891. Abstracted in Deutsche med. Wchnschr. 80: 772, 1892.

9 Metchnikoff: Pathologie comparée de l'inflammation. Paris, G. Masson, Éditeur, 1892.

10 Vaughan, V. C.; Novy, F. G. and McClintock, C. T.: The germicidal properties of nucleins. Medical News. 62: 536, 1893.

11 Ames, D., and Huntley, A. A.: The nature of the leukocytosis produced by nucleinic acid. A preliminary experimental study. J. A. M. A. 29: 472, 1897.

12 Jackson, Henry Jr., and Parker, Frederic Jr.: The treatment of malignant neutropenia with pentose nucleotides. J. A. M. A. 97: 1436 (Nov. 14) 1931.

13 Milroy, T. H., and Malcolm, J.: The metabolism of the nucleins. J. Physiol. 25: 105, 1899.

14 Habetin, P.: Über Funktionsprufüng des Knochenmarkes. Wien. Arch. f. inn. Med. 7: 329 (Dec.) 1923.

15 Jackson, Henry Jr.: Studies in nuclein metabolism. The isolation of a nucleotide from human blood. J. Biol. Chem. 59: 529 (April) 1924.

16 Larsell, O.; Nokes, H. T., and Phillips, B. I.: Hemopoietic effect in rabbits of intravenous injection of cells, nuclei, and nucleic acids from blood of fowls. Arch. Path. and Lab. Med. 2: 698 (Nov.) 1926.

17 Doan, C. A.; Zerfas, L. G.; Warren, S., and Ames, O.: Study of mechanism of nucleinate-induced leucopenic and leucocytic states, with special reference to the relative rôles of liver, spleen and bone marrow. J. Exp. Med. 47: 403 (Mar.) 1928.

18 Reznikoff, Paul: Neucleotide therapy in agranulocytosis. J. Clin. Inv. 9: 381 (Dec.) 1930.

19 Jackson, H. Jr.: Agranulocytic angina. Med. Clin. N. Am. 16: 973 (Jan.) 1933.

AGRANULOCYTOSIS. REPORT OF THREE CASES TREATED WITH NUCLEIC ACID DERIVATIVES*

BY WILLIAM DAMESHEK, M.D.†

THE treatment of agranulocytosis has become completely revolutionized since Reznikoff[1] in 1930 first suggested the use of nucleic acid derivatives as therapeutic agents. This worker used salts of the relatively simple purine bases adenine and guanine (adenine sulphate and guanine hydrochloride) in treating four patients, three of whom recovered. The efficacy of the purine bases in elevating the white blood cell count had previously been demonstrated in the carefully controlled animal experiments of Doan, Zerfas, Warren and Ames[2]. Jackson, Parker, Rinehart and Taylor[3] later used the "unbroken" pentose nucleotides in a series of twenty cases of severe neutropenia, fourteen of which recovered. In the latters' second series of sixty-nine cases[4], recovery occurred in 74 per cent. Doan[5], from a review of forty-four cases treated with nucleic acid derivatives, found that thirty-three recovered. Before treatment with nucleic acid derivatives was instituted, the mortality rate for the disease varied from 80-90 per cent[6]; at present it is about 25 per cent[5]. There can be no doubt, therefore, that this specific method of therapy has considerably lowered the mortality rate of a once almost hopeless disease.

The three cases reported below are interesting from several standpoints: (1) they were all relapsing or recurrent in type and showed characteristic onsets; (2) they all recovered after treatment with nucleic acid derivatives was instituted; (3) in one case, the effects of adenine sulphate and of pentose nucleotides in different relapses could be compared; (4) complete hematological studies were carried out; (5) certain reactions to pentose nucleotides were noted.

REPORT OF CASES

CASE 1. Emily D. T. Seen with Dr. H. J. Inglis of Boston.

This case in its first serious relapse was reported in a previous paper[7]. A woman, aged 48 years, had had numerous attacks of tonsillitis, bronchitis and asthma for many years. In November, 1929, she began to feel very tired and weak and finally on December 8, took to bed. On December 10 she developed a severe sore throat and a sore mouth and on the following day a membrane was noted on one tonsil. From December 10 to December 24 her condition became progressively worse and on the latter date she was moribund and had tracheal râles. Several areas of ulceration covered with grayish-white membrane were present on the gums, buccal mucous membranes, tongue, and tonsils. The white blood cell count was 1500 per cu. mm., polymorphonuclear cells 1 per cent, lymphocytes 99 per cent. On December 25, the patient was given a transfusion of 500 cc. of blood, 10 cc. of whole milk intramuscularly and large amounts of fluid intramuscularly and by rectum. There was rapid clinical and hematological improvement, the leukocyte count on December 27 being 8000 per cu. mm., the percentage of polymorphonuclear cells gradually returning to normal limits.

The patient was well until May 23, 1932 when she began to weep unrestrainedly while visiting a cemetery. That evening she had a severe chill, not associated however with fever. She became weak and depressed and wept almost constantly. Various physicians treated her without relief. Weakness became extreme; she was unable to eat on account of numerous "sores" in the mouth and throat. Fever developed and finally on June 9, Dr. Inglis was called at the patient's request, since she herself suspected the presence of her previous disease. Dr. Inglis found the white blood cell count to be 2400 per cu. mm. with granulocytes absent. On June 10, when I saw the patient, she was prostrated and had a temperature of 103°F. Several ulcerating lesions covered with heavy grayish-white membrane were present on the gums, buccal mucous membranes, and pharynx. She was immediately given an injection of pentnucleotide, 10 cc. intramuscularly. During the next four days she was given two injections daily; on the three succeeding days, she received daily injections. Definite hematological improvement was noted on June 13, about 72 hours after treatment was begun—myelocytes and metamyelocytes appearing in the peripheral blood. Clinical improvement was slower, the temperature rising frequently to 104°F. There was constant vertigo and headache, the joints were painful, the eyelids, particularly the left one, became markedly swollen, and there was slight incontinence of urine, and confusion. It was thought that some of these ymptoms were related to the injections of nucleotide, and that the swelling of the eyelids and of the upper part of the nose was associated with acute ethmoiditis. On June 16 the patient was definitely improved. On June 18, the leukocyte count reached its peak: 16,800 per cu. mm., and on June 20, the patient was discharged from the hospital feeling well except for slight pain in both buttocks, especially in the left. On June 30, there was marked swelling in the left gluteal region and on July 4 an abscess of the left buttock was incised and drained. Since then, the patient has been well, the leukocyte count fluctuating between 8000 and 9000 per cu. mm.

CASE 2. Rose S. B. I. H. 11,575. Reported through the courtesy of Dr. Hyman Morrison of Boston.

This unmarried woman, aged 44 years, entered the Beth Israel Hospital on July 23, 1931 with severe sore throat, high fever and prostration. She had "never" been strong, was usually "nervous" and was subject to frequent spells of indigestion and migraine. In 1925, hysterectomy was performed for fibroid uterus. In 1920 and 1929 she had attacks of pneumonia; twice between those dates she had been ill with "grippe". All of these illnesses had been preceded by sore throat. During the latter part of June, 1931, she had been in bed for about ten days with fever and sore throat. Although she did not feel entirely strong, she returned to work. On July 19, she developed malaise, sore throat, and swelling at the left side of the neck. These symptoms rapidly became worse; prostration developed

*From the Medical Clinic and Department of Pathology, Beth Israel Hospital, Boston.

†Dameshek—Associate Physician, Beth Israel Hospital, Boston. For record and address of author see "This Week's Issue," page 1070.

and the patient was admitted to the hospital. There was marked difficulty in opening the mouth, so that the buccal cavity and the pharynx were not well seen; however, ulcerating lesions of the gums covered with grayish membrane could be seen. A hard, tender, walnut-sized mass was felt below the left ear. The temperature ranged between 102-103°F., the pulse 150 per minute. The blood showed slight hypochromic anemia (hemoglobin 65 per cent, red blood cell count 4.72 millions per cu. mm.), the blood platelets were normal in number (811,000 per cu. mm.) but the leukocyte count was only 800 per cu. mm. with four per cent polymorphonuclear cells being present. On the morning of July 24, she was given 0.5 Gm. adenine sulphate intravenously. On the same afternoon the white blood cell count had risen to 2800 and during the following day it rose to 13,000 with 95 per cent polymorphonuclear cells. Coincident with this, the temperature rose to 105°F. and patchy areas of consolidation were discovered in the lungs. Blood culture showed a growth of pneumococci, identified as Type IV. From July 26 to August 3, the leukocyte count ranged from 18,500 to 25,000 per cu. mm. The mouth lesions rapidly cleared as did the signs of pulmonary consolidation. The mass at the left side of the neck became fluctuant and was incised on August 1, and finally on August 13, 1931, the patient was discharged from the hospital.

She was well during the summer and fall of 1931. On December 23, 1931, she developed a sore on the tongue; sloughing soon took place with the formation of a moderately large ulcer on the left anterior portion. Again marked weakness developed and there was fever and sore throat. The leukocyte count on December 30 was 2000 per cu. mm. At this time she was given injections of pentnucleotide intramuscularly daily for five days, the leukocyte count rising to 3600 per cu. mm. on the fourth day. Again cervical adenitis developed and again incision and drainage of a cervical abscess became necessary. The patient was in bed for 21 days, after which convalescence in a warmer climate was advised.

In February, 1932, the patient went to Florida. She felt well for about a week, but then began to feel tired, sleepy, and depressed. She wept almost constantly for two days and on the third day noticed a small blister on the upper lip. This soon became infected and cellulitis of the right side of the face developed. The leukocyte count was 2500 per cu. mm. and she was again given pentnucleotide intramuscularly. In April and May, coincident with sensations of weakness and depression, she developed purulent lesions about several finger nails. From July 21, 1932, to the present she has been seen frequently in the Blood Clinic of the Beth Israel Hospital. During this period, the leukocyte count has fluctuated from 1600 to 8300 per cu. mm., the polymorphonuclear cells from 19 to 63 per cent. She has usually been able to foretell the approximate level of her leukocyte count by her subjective sensations. With a very low leukocyte count, she feels tired and depressed; with a more normal count, her energy is greater and her spirits better. Since this paper was written, the patient developed another severe relapse associated this time (Sept. 20, 1933) with an infection of a toe. Again, striking improve-

Table I.

Case 1. Mrs. Emily D.T.

		W.B.C. per cu. mm.	Total Polymorphs. %	Metamyelocytes %	Myelocytes %	Lymphocytes %	Monocytes %	Histiocytes %	Eosinophiles and Basophiles
Relapse I.	12/24/29	1,500	1			99			
	12/25/29	10,000 (?)							
	12/27/29	8,000	22	18	-	50	28	9	
	12/29/29	7,600	43.2	32.4	1.2	45.2	11.6	1.2	
	1/1/30	-	38	16	-	40.5	21.5	-	
	1/4/30	-	50	8.5	-	35.5	14.5	-	
Relapse II	6/9/32	2,400	0		-	100			
	6/10/32	4,200	1	1		74	25	1	Pentnucleotide begun
	6/11/32	4,700	0			65.5	34.5		
	6/12/32	3,700	1			85.0	14.0		
	6/13/32	3,800	10	5	4	63	27.0	1	
	6/14/32	10,800	26	16	4	60	14.		
	6/15/32	11,400	64	47		31	5		
	6/16/32	13,600							
	6/18/32	16,800	63	18.5		34	3		
	6/20/32	10,400	57	12		39	4		
	6/30/32	13,400							
	7/20/32	8,400							
	8/9/32	9,000							

ment occurred following the immediate administration of pentnucleotide intramuscularly.

CASE 3. Charles C. B. I. H. 14,369; 14,473. Seen with Dr. Max Jacobs of Boston.

This machinist, aged 47 years, was admitted to the hospital on April 27, 1932, for a radical operation of the maxillary antrum. Since boyhood he had been subject to annual attacks of "grippe", lasting usually from two to six weeks, occurring either in the winter or spring, and always associated with high fever, sore throat, and prostration. In 1925, several teeth were extracted; healing took place very slowly, however, and was complete only after seven weeks. One year before admission he began to notice increasing fatigue, gradually progressing to marked debility. Six weeks before admission, several teeth were extracted since they were suspected of being "foci of infection". The gums failed to heal and a foul discharge from an upper molar tooth socket developed. On April 27, 1932, radical operation of the right maxillary antrum was performed by Dr. Jacobs. The wound failed to heal properly, fever developed, and the patient became prostrated. On May 7, 1932, he was readmitted to the hospital in a state of prostration and semidelirium with a rectal temperature of 105.5°F. There was slight icterus of the sclerae; several ulcerative lesions covered with grayish-white adherent exudate were present on the gums, the buccal mucous membranes, tooth sockets, and tonsillar fossae. Leukocyte count on May 8 was 3200 per cu. mm., no polymorphonuclear cells being present. Pentnucleotide 10 cc. was given at 11:30 P.M. on May 8. On the following morning, 10 cc. of pentnucleotide diluted with normal salt solution was given intravenously. This injection was followed by a severe chill, temperature of 106°F., and a sensation of tightness in the chest. The leukocyte count fell to 2200 per cu. mm. on the morning of May 10, polymorphonuclears still being absent. However, on the afternoon of May 10—less than 48 hours after the institution of nucleotide therapy—five per cent of polymorphonuclear cells were seen, all of them being either myelocytes or metamyelocytes. Although the temperature rose to 104.2°F. on that day, there was continued and rapid clinical and hematological improvement. He was given pentnucleotide twice daily intramuscularly until May 15, and daily thereafter until May 19. On the latter date, leukocyte count was 16,100; polymorphonuclears 63 per cent. A marked increase in discharge from the maxillary sinus was noted when the white blood cell count had risen to normal limits. In July 1932, the patient returned to work. Since then, his leukocyte count has fluctuated between 6400 and 8200 per cu. mm.

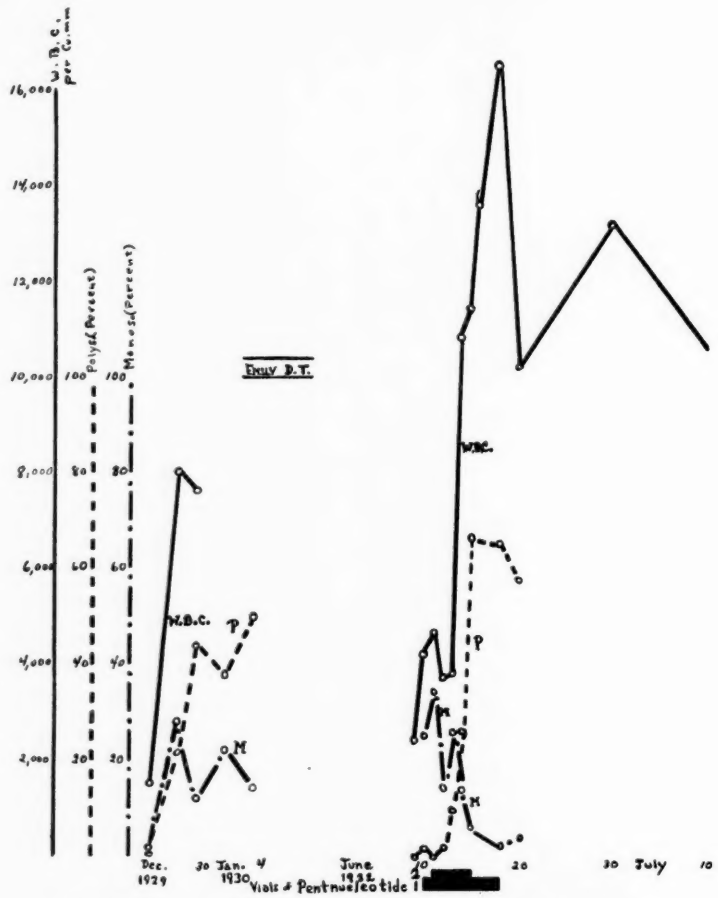


CHART 1. Emily D. T., Case 1. A relapsing case of agranulocytosis. In 1929 the patient improved with non-specific therapy. In 1932 there was striking improvement with the use of pentnucleotide. Note the marked increase in monocytes (M) and their diminution as the polymorphonuclear cells (P) became increased. Immature polymorphonuclear cells appeared seventy-two hours after treatment was begun in the second relapse.

DISCUSSION

1. *The Relapsing or Recurrent Tendency*

It appears that the more this disease is studied, the greater is the incidence of relapsing or recurrent cases. Since the disease was first described, note has usually been made of its occurrence in individuals who had been subject to numerous illnesses in the past and who were more or less debilitated. The significance of these numerous past illnesses did not appear until it was possible to study patients in repeated relapses. The suggestion was then advanced that the disease was a fundamental one of granulocyte formation in the bone-marrow and that the ulcerative lesions of various mucous membranes might not be the primary disorder but rather a secondary infectious manifestation resulting from a chronic or recurrent "neutropenic state[8]". It appears that certain individuals are frequently on the border-line of agranulocytosis, and several have been observed to develop the typical features of the disease after a few days of complete absence of granulocytes from the peripheral blood[8]. These individuals apparently possess a bone-marrow which is defective in the production of granulocytes. This defect may be chronic or cyclic,

Case 2- Miss Rose S. TABLE II.

	1931	Hemoglobin %	R.B.C. Millions	W.B.C.	Total Polymorphs. %	Lymphocytes %	Monocytes %	Remarks
Relapse I.	July 23	65	4.72	800	4	96		
	July 24 a.m.			800	59	35	6	Adenine sulphate 0.5g. intravenously
	p.m.			2800	68	22	10	
	July 25 a.m.		4.18	5500				
	p.m.			13000	95	5		
	July 26			21000	90	9	1	
	July 27			19800	84	10	6	
	July 28			31100				
	July 29			13400	87	10	3	
	July 30			24800	71	26	3	
	Aug. 3			24400	89	10	9	
	Aug. 4			21700				
	Aug. 6			16700				
	Aug. 10			11400				
	Aug. 12			8800				
Relapse II.	Dec.30,'31			2000		78	22	Pentnucleotide 0.7 daily begun
	Dec. 31,'31			2300		90	10	
	Jan. 1,'32			2800				
	Jan. 2,'32			3000				
	Jan. 3,'32			3600				
	Jan. 4,'32			4000	29	56	14	
	Jan. 5,'32			4400				
	Jan. 6,'32			5000	30	62	8	
Relapse III	Feb. 1932			2500				Pentnucleotide given
								Immature Polymorphs. %
Neutropenia	July 21	70	5.02	2,600	48	49	3	15
	July 27			1,600	19	81	0	8
	Aug. 3	75		2,250	62.7	36	1.3	28
	Aug. 10			4,600				
	Aug. 17			2,800	57	42	1.	
	Aug. 24			4,000	59	36	5.	12
	Sept. 8			3,200	49	48	2	15

but when it becomes marked it is probable that various infections, usually buccal or pharyngeal, develop and lead to the disease complex known as agranulocytosis or malignant neutropenia. Various authors[5, 8] have emphasized that the patient may feel differently when the leukocyte count is low than when it is normal. Thus the vague symptoms of weakness, easy fatigability, drowsiness and mental depression may be said to characterize the neutropenic state. This is well brought out in Case 2 of this series. varying period of mental depression, lack of energy, and marked fatigue. In Case 3, there was gradually increasing fatigue leading to actual debility before fever finally developed.

2. *Treatment with Nucleic Acid Derivatives*

The outlook for the patient with agranulocytosis has been made immeasurably brighter since Reznikoff[1] first suggested and Jackson[3] then developed the treatment with nucleic acid derivatives. Doan[2] and his co-workers should

Table III.

Case 3. Mr. Charles C.

	Hemoglobin %	R.B.C.	W.B.C.	Total Polymorphs. %	Metamyelocytes %	Myelocytes %	Lymphocytes %	Monocytes %	Eosinophiles and basophiles %	Remarks
May 8 a.m.										
p.m.	80	4.45	3,200	0			41	59		Pentnucleotide begun
May 9 a.m.										
p.m.			2,700	0			33	56	1	
May 10 a.m.			2,200	0						
p.m.			2,500	5	3	2	54	39	2	
May 11 a.m.			3,200	32	22	6	41	35	0	
p.m.			3,500	52	40	6	28	19	0	
May 13 a.m.	70	4.10	6,500	48	30	2	30	19	0	
p.m.			6,200	63	34	2	21	14	1	
May 14			8,800	74	30	2	21	4	1	
May 16			8,900	73	22	1	23	4		
May 17			8,700	78	16	0	16	5	1	
May 19	65	4.10	16,100	65	10	0	29	6	0	pentnucleotide discontinued
June 4			8,800	78	4	0	18	4	0	
Sept. 8			7,200	70	2	0	21	8	1	

Definite relapses were noted in two of the patients of this series. In Case 1, the patient was well for more than two years between relapses. Her frequent attacks of "tonsillitis" and "grippe" in the past might have been on the basis of agranulocytosis. In Case 2, the patient has had frequent relapses during the past two years; here, too, it is possible that some of her previous illnesses might have been associated with severe neutropenia. In Case 3, although no definite relapses were studied, it seems probable that the annual attacks of fever, sore throat, and prostration lasting from six to eight weeks and diagnosed as "grippe" were actually mild attacks of agranulocytosis. The failure of the gums to heal after dental extraction in 1925 may have been on this basis.

The onset in these cases was fairly characteristic. In Case 1, the first relapse was preceded by a long period of weakness, her second relapse by a period of severe depression and weakness. In Case 2, each relapse was heralded by a

be credited with their long and careful experimental work which undoubtedly led to the use of this mode of therapy. Jackson and co-workers[4] were able to collect a group of 54 typical cases in which treatment with pentose nucleotides had been given; 38, or 70 per cent of these recovered. In 13 patients treated by Reznikoff with adenine sulphate, ten recovered (77 per cent). These figures may be compared with those of the "pre-nucleotide era" in which the *mortality* was variously estimated as between 75 and 95 per cent. In 1931, I reported a series of nine cases with two recoveries[7]; the recovery of these two cases was stressed as being somewhat unusual. In this very small group of three consecutively treated cases, all recovered. The approximate date of recovery from the beginning of treatment has furthermore become predictable. Jackson, Parker and Taylor[4] have brought out in their series of cases (treated by different individuals in various parts of the country) that irrespective of how long the pa-

tient had had the disease, "unequivocal" clinical and hematological response took place on the fifth day of treatment.

Of the present group, in Case 1, definite hematological response took place 72 hours after

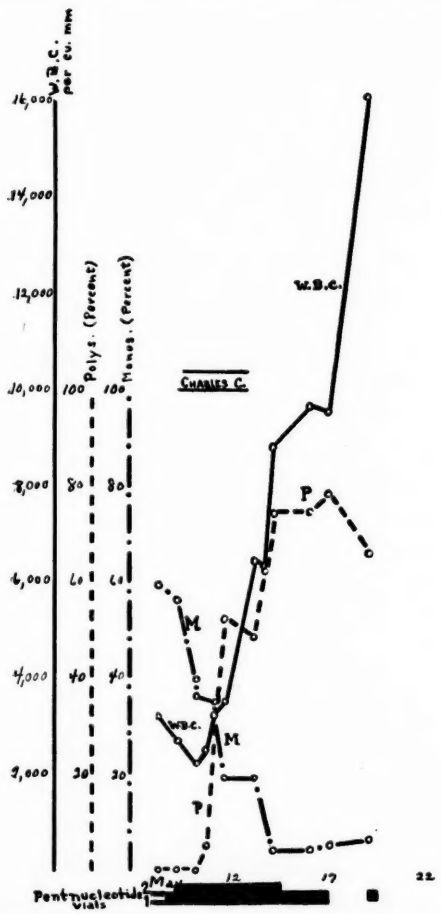


CHART 2. Charles C., Case 3. Effect of pentnucleotide in a case of agranulocytosis. Note the marked increase in monocytes (M) and their diminution as the percentage of polymorphonuclear cells (P) increased. Imature polymorphonuclear cells were noted within forty-eight hours after treatment was begun.

treatment was begun, clinical improvement being somewhat slower. In Case 2, with adenine sulphate, there was striking hematological improvement within eight hours, clinical improvement taking place with subsidence of bronchopneumonia in 72 hours. At another relapse in the same case when pentnucleotide was given, clinical improvement was noted in less than 48 hours after the beginning of treatment, definite hematological improvement being present in about 72 hours. These somewhat more rapid responses than those noted by Jackson *et al* have also been commented upon by Blake[10] who noted initial response at 48 hours, and by Doan[5].

Yeast nucleic acid is made up of four nucleotides. A solution of the sodium salts of these nucleotides was introduced by Jackson *et al*[3]. Each of these nucleotides is in turn composed of a purine of pyrimidine base linked with the saccharide pentose, and with phosphoric acid. The purine or pyrimidine bases may be broken off from their linkages with pentose and phosphoric acid, and it is these purine bases, adenine and guanine, that Reznikoff[1] used for intravenous therapy. These appear to be at least as efficacious as the mixture of unbroken pentose nucleotides so that it is entirely possible that the active principle effective in therapy may be one or several of the purine bases formed in the body after intramuscular injection of the "unbroken" nucleotides.

In Case 2, it was possible to compare the effects of the two materials in the same patient at different relapses. The results are to be sure not strictly comparable, since at the first relapse there was a complicating bronchopneumonia. The adenine sulphate intravenously caused no apparent reaction. As noted above, the leukocyte count had become doubled within eight hours and there was rapid clinical and hematological improvement. Improvement at the second relapse when pentnucleotide was given was slower, although the patient seemed less ill. Reznikoff[11] states that response to adenine sulphate treatment usually begins within 24 hours. McLester and Parsons[12] treated two patients with adenine sulphate and noted "immediate and marked improvement". From the above observations and from observations of Reznikoff, the two preparations may be compared:

It may be said that at the present writing the mixture of pentose nucleotides is more readily available to the practising physician and easier to handle. At any rate, in both adenine sulphate and in the mixture of pentose nucleotides we now have potent weapons against what was considered until very recently an almost

Table IV. Comparison of Adenine Sulphate and Pentnucleotide.

	Chemical Nature	Solubility	Mode of Treatment	Reaction	Rapidity of Action	End Result (Recoveries)
Adenine Sulphate	Relatively simple purine base	Slowly soluble	Intravenously	Very rare	Within 24 hours	About 75%
Pentose Nucleotides	Mixture of more complex molecules	Easily soluble	Intramuscularly, occasionally intravenously	Usually	48-140 hours	About 75%

hopeless disease. These nucleic acid derivatives appear to be of specific value in the treatment of agranulocytosis and may be compared in specificity with liver extract in pernicious anemia and insulin in diabetic coma. They apparently have a specific action on the formation of bone-marrow granulocytes and thus attack what is probably the essential cause of the disease: defective formation of granulocytes in the bone-marrow. The many failures which are being informally reported are probably due to the use of the drug in conditions of leukopenia not "primary" in type but secondary to severe sepsis, aplastic anemia, or aleukemic leukemia.

3. *Reactions*

In the description of "pentnucleotide" in New and Non-Official Remedies[13] the following statement is made regarding reactions: "Immediately following the intravenous administration of pentnucleotide there is usually a sharp, temporary reaction characterized by dyspnea, precordial distress, bradycardia, and sweating. Following intramuscular use, similar reactions have occasionally been reported but in milder form; generally no reaction occurs." Jackson *et al*[4] made essentially the same observations.

In Case 1 of this series, there was a definite reaction following each intramuscular treatment with pentose nucleotides. After the first injection, there was a severe chill, the temperature dropping to 98.6°F. Although no chills developed after the other injections, it was thought that the frequent and irregular rise in temperature to 104°F. was associated with them. Shortly after each injection, the pationt felt as though her "body was burning up". She became generally itchy and had a sense of impending death. This was followed by a sense of complete "let-down", and extreme weakness. For about 45 minutes thereafter, the patient was confused, acted peculiarly, and seemed listless and lethargic. At the end of an hour, the immediate symptoms of the reaction were gone. Whether the painful joints which the patient complained of were associated with the use of pentnucleotide could not be determined. As noted above, an abscess of one of the buttocks developed, necessitating surgical drainage. Whether this was due to infection introduced with the needle or to simple trauma of muscle fibers, which in the absence of granulocytes led to abscess formation, could not be determined. Culture of the purulent material from the abscess cavity was sterile.

In Case 2, the reactions following pentnucleotide therapy were not studied. It was possible to study carefully the reactions occurring in the relapse of September, 1933. These were closely similar in type to the reactions noted in Case 3 described above. In Case 3, there was a severe reaction following the intravenous use of pentnucleotide. Severe chill occurred, temperature rising to 106°F. and dropping to 98°F. in six hours. Simultaneously there was a tight sensation in the chest, which was relieved by the subcutaneous injection of atropine sulphate. Following each intramuscular injection of pentnucleotide the following reaction occurred: a few seconds after injection, there was a "tight" sensation in the chest, a feeling of "inward excitement" and then "tension" of the entire body. This was followed by a profound feeling of "let-down", semi-stupor, and dullness lasting for 30-60 minutes. If questioned during this period, the patient would answer, if at all, slowly and listlessly. At the end of an hour, no unusual sensation was present. The same type of reaction occurred whether the leukocyte count was low or normal.

In the one case in which adenine sulphate was used intravenously, no reaction was noted. Reznikoff[11] writes that he noted only two reactions in a series of about 200 consecutive intravenous injections of adenine sulphate. In one of these reacting cases, the medication was inadvertently given intramuscularly; in the other, a transfusion of blood was given at the same time as the injection.

4. *The Hematological Response to Treatment*

In previous papers, I have described the hematological response occurring in cases of agranulocytosis (1) during spontaneous recovery[7] (2) following transfusion and injection of foreign protein[7] and (3) in rabbits following the injection of *Salmonella suipestifer* in the attempt to produce the typical blood-picture experimentally[14]. Marked similarity in the type of response occurring during recovery was noted. Briefly, the following hematological changes occurred in orderly fashion: (1) histiomonocytosis (2) appearance of increasing numbers of immature granulocytes (3) rise in white blood cell count, appearance of mature granulocytes, diminution of monocytes. The identical response was seen in two of the cases reported in this paper during the recovery phase following the injection of nucleic acid derivatives.

The stages of (1) histiomonocytosis (2) increase in mature granulocytes with concomitant reduction in mature granulocytes and (3) lymphocytosis are seen during the recovery from almost all acute infections[15]. They may also be brought about by the injection of various foreign proteins such as typhoid vaccine, milk, and by inert material such as India ink, gentian violet, etc.[16]. The response of the blood-forming organs to various infections, toxins, and foreign materials thus appears to be "standardized". I have been particularly interested in the phase of monocytosis and have described the appearance of histiocytes (which are probably the

forerunners of the normal blood monocytes) in the peripheral blood during the convalescence from acute infections, agranulocytosis, etc.[17]. The appearance of these cells during the phase of monocytosis is probably indicative of a hyperactive reticulo-endothelial system. This system, as I have previously suggested[17], may represent a "second line of defense" against infection, the "first line" being the polymorphonuclear cells of the bone-marrow. Cases 1 and 3 of the present series presented a marked monocytosis before treatment with nucleotides was begun, the percentage of these cells gradually diminishing with recovery. It is tempting to speculate that with inactivity of the "first line of defense" (the granulocytes) the "second line of defense" (the reticulo-endothelial system, the monocytes) may take up the brunt of the burden. The reciprocal relationship of the monocytes and of the polymorphonuclear cells is brought out in the accompanying charts.

The appearance in the peripheral blood of definite numbers of immature polymorphonuclear cells marks the onset of definite hematological improvement. These cells appear in the order of their formation in the bone-marrow, i.e., myelocytes (at times myeloblasts) are seen first, after which appear large numbers of metamyelocytes for several days; the latter gradually give way to mature polymorphonuclear cells. The total white blood cell count becomes elevated a day or two after immature granulocytes are seen in the peripheral blood. (This is reminiscent of the elevation of red blood cell count after the appearance of immature red blood cells—reticulocytes—in the blood-stream.) The leukocyte count rises rapidly after its initial increase, and counts of 18,000 to 20,000 per cu. mm. are not uncommon within seven to ten days after the beginning of therapy.

Jackson[4] has stated that no definite clinical or hematological improvement occurs until about the fifth day after beginning the treatment with nucleotides. In the group of cases reported in this paper, hematological improvement became noticeable in Case 1 seventy-two hours after treatment was begun, in Case 2 eight hours after treatment (with adenine sulphate), in Case 3 thirty-six hours after treatment was instituted. Blake[10], in discussing Jackson's paper at the 1932 meeting of the Association of American Physicians, stated that in his experience the initial response to treatment with adenine sulphate occurs within twenty-four hours, occasionally within six hours. It is probable (1) that the response to intravenously injected adenine sulphate is more rapid than to that of pentose nucleotides given intramuscularly and (2) that more careful study will, as Jackson states, demonstrate a beginning response at a time much earlier than five days after the onset of therapy.

SUMMARY

A group of three patients with cyclic or relapsing agranulocytosis is described. The following features are emphasized: (1) the relapsing or recurrent tendency (2) the striking and "specific" response to nucleic acid derivatives (3) the reactions following treatment with pentnucleotide (4) the hematological response, with particular reference to the histiomonocytosis, which occurs during recovery. It is concluded that the relatively simple nucleic acid derivative adenine sulphate, and the more complex mixture of pentose nucleotides are both highly effective and probably specific in the treatment of true agranulocytosis. The adenine sulphate may represent the active principle in the mixture of pentose nucleotides.

REFERENCES

1 Reznikoff, Paul: Nucleotide therapy in agranulocytosis. J. Clin. Investigation. 6:16, 1930.

2 Doan, C. A., Zerfas, L. G., Warren, Sylvia, and Ames, Olivia: A study of the mechanism of nucleinate-induced leucopenic and leucocytic states, with special reference to the relative rôles of liver, spleen, and bone marrow. J. Exper. Med. 47:403, 1928.

3 Jackson, Henry, Jr., Parker, Frederic, Jr., Rinehart, J. F., and Taylor, F. H. L.: Studies of diseases of the lymphoid and myeloid tissues. VI. The treatment of malignant neutropenia with pentose nucleotides. J. A. M. A. 97: 1436 (Nov. 14) 1931.

4 Jackson Henry, Jr., Parker, Frederic, Jr., and Taylor, F. H. L.: Studies of diseases of the lymphoid and myeloid tissues. VII. The nucleotide therapy of agranulocytic angina, malignant neutropenia and allied conditions. Am. J. M. Sc. 184:297, 1932.

5 Doan, C. A.: The neutropenic state. J. A. M. A. 99:194 (July 16) 1932.

6 Kracke, R. R.: A review of granulocytopenia (agranulocytosis). J. Lab. & Clin. Med. 17:993, 1931-32.

7 Dameshek, William, and Ingall, Maurice: Agranulocytosis (malignant neutropenia). Am. J. M. Sc. 181:502, 1931.

8 Roberts, S. R., and Kracke, R. R.: Agranulocytosis; report of a case. J. A. M. A. 95:780 (Sept. 13) 1930.
Harkins, Henry: Granulopenia and agranulocytic angina. J. A. M. A. 99:1132 (Oct. 1) 1932.

9 Reznikoff, Paul: Discussion of the treatment of agranulocytosis. Association of American Physicians, 1932 meeting, Atlantic City, May 3 and 4, 1932. Reported in J. A. M. A. 99:163 (July 9) 1932.

10 Blake, F. G.: Discussion of the treatment of agranulocytosis. Ibid.

11 Reznikoff, Paul: Personal communication.

12 McLester, J. S., and Parsons, W. H.: The treatment of granulopenia with nucleotide derivatives. Association of American Physicians, 1932 meeting. Ibid.

13 Report on pentnucleotide. New and Nonofficial Remedies. J. A. M. A. 99:1175 (Oct. 1) 1932.

14 Fried, B. M., and Dameshek, William: Experimental agranulocytosis. Infection of rabbits with salmonella suipestifer by way of the blood stream. Arch. Int. Med. 49:94, 1932.

15 Schilling, V.: The Blood Picture. American Edition. St. Louis, C. V. Mosby Co., 1929.

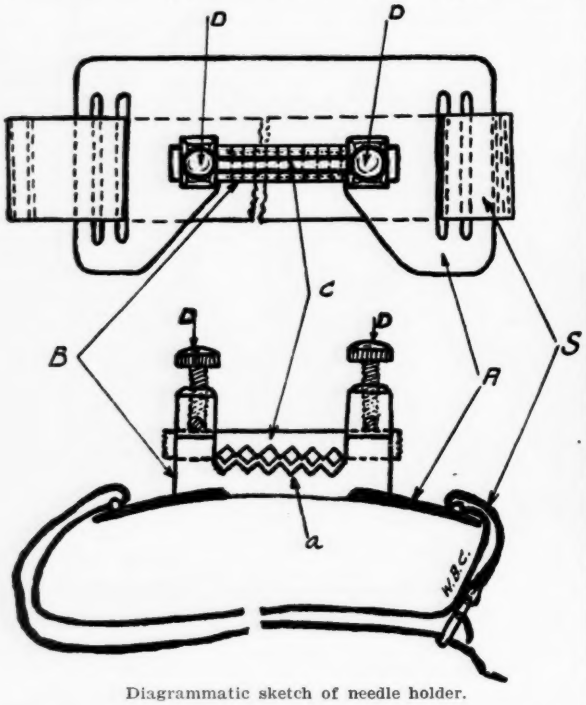
16 Dameshek, William: Unpublished data.

17 Dameshek, William: The appearance of histiocytes in the peripheral blood. Arch. Int. Med. 47:968, 1931.

NEEDLE HOLDER FOR BLOOD TRANSFUSION AND INTRAVENOUS THERAPY

BY WELMAN B. CHRISTIE, M.D.*

DURING a blood transfusion much difficulty is often encountered in holding the needle in the vein of both the donor and the recipient. As a result, a simple surgical procedure is thereby made very difficult, and at times nearly impossible. The same difficulties occur in the giving of other intravenous therapeutic agents as normal saline, glucose, etc., where large amounts

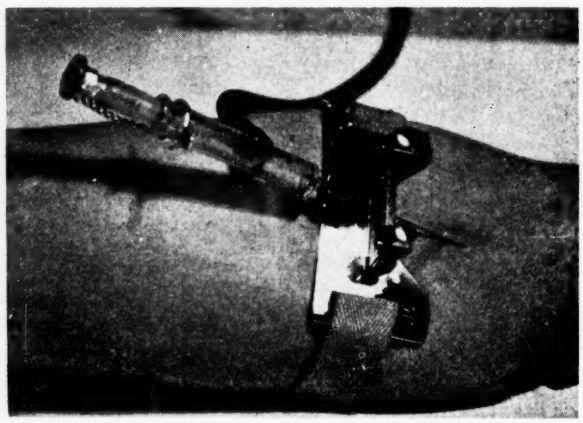


Diagrammatic sketch of needle holder.

are needed and the necessity of giving them slowly is paramount. Especially is this true in the use of the continuous intravenous drip where the needle is kept in the vein for quite some time.

With these difficulties in mind the following holder was designed in an effort to simplify this part of an important therapeutic measure. So far as I have been able to learn, no similar device has been described in the literature, or used by the medical profession.

The instrument consists of a curved metal frame piece, A, on the upper surface of which is a double frame piece, B, with teeth cut across it at a. The angle of inclination of these teeth is toward the area which is cut out of A. This latter side of the frame piece is the area that is placed nearest the point of entry into the vein. The teeth being set at this angle give the needle the necessary tilt when it is placed between these teeth and the teeth in the adjustable bar, C, which is locked firm against the needle by thumb screws, D.D. This single adjustable, toothed bar, when locked down will hold any size needle very firmly and without any lateral or up and down play. The adjustable strap, S, will hold the adapter on the arm without constricting the blood supply, and it may be placed across the arm at any angle, depending on the direction of the vein to be used.



Holder used with a fine gauge needle attached to an intravenous infusion syringe.

The photograph shows its use with a fine gauge needle attached to an ordinary intravenous infusion syringe, but, as stated above, it will hold a needle or trocar of any size. Of course, in the giving of a continuous intravenous drip where the needle is to be kept in the vein for many hours, some method of holding the arm in an extended position is desired. This may easily be accomplished by an ordinary pillow splint. With the holder in place, and the needle in the vein, the arm may be moved in any plane or direction at the shoulder without interfering with the intravenous operation, flexion at the elbow being the only arm motion that affects it. With the use of this simple holder a blood transfusion can easily be a one man operation, and the use of unsterile adhesive strappings holding the needle in a continuous drip can be discarded.

NOTE: This holder was made for the author by the Codman Shurtleff Company, of Boston, to whom I wish to express my thanks for their valuable help and suggestions.

*Christie—Second Assistant Visiting Surgeon, Massachusetts Memorial Hospitals, Boston. For record and address of author see "This Week's Issue," page 1070.

CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

EDITED BY RICHARD C. CABOT, M.D.
F. M. PAINTER, A.B., ASSISTANT EDITOR

CASE 19471

MARKED CEREBRAL SYMPTOMS FOLLOWING A LIMP OF THREE MONTHS' DURATION

CHILDREN'S MEDICAL DEPARTMENT

PRESENTATION OF CASE

DR. MARGARET E. MORIARTY:* An eight year old American born boy was admitted to the hospital.

Family history. The father, mother and five siblings were well. One brother has a congenital dislocation of the lens.

Past history. The patient was born spontaneously, although the labor was rather long. He appeared normal at birth, showing no rash, cyanosis, snuffles or convulsions. He was fed by bottle. Cod liver oil was given sporadically, orange juice daily. His gain in weight and development were slow. He cut his first teeth at eight months, sat up at seventeen months, walked at two years and talked at three years. He had attended kindergarten but had been refused admission to the grades.

He had diphtheria at seventeen months, whooping cough at five years, mumps at six and measles at seven. The lenses of both eyes were congenitally dislocated. He was operated on at the Eye and Ear Infirmary for this two years before admission. An operation for tonsillectomy and adenoidectomy was done at three years of age. He had treatment for flat feet at another hospital. He had never seemed very bright; his mother thought his eyes may have been responsible.

Two weeks before admission he was brought to the Orthopedic Outpatient Department because of a limp which had first appeared three months previously. There was no apparent cause and no associated pain or illness. The limp had disappeared in one week, to reappear two weeks before the Outpatient admission. Examination showed a marked left leg limp with atrophy of the left lower leg with 5/8 of an inch shortening. All motions of the leg were accompanied by muscle spasm, which, however, was overcome by gentle traction. X-ray of the hip was taken ten days before admission. His hip was put in a plaster cast. His appetite was not good and he was quite constipated, requiring frequent enemata.

*Resident on the Children's Medical service.

Present illness. Four days before admission the child began to have vomiting, not projectile. That day he vomited everything taken, water, orange juice, crackers, etc. He continued to vomit rather frequently. The day before entry he began to complain of generalized headache. There had been no convulsions, but rather frequent twitchings of various parts of his body. With the exception of enuresis there had been no genito-urinary symptoms. For the past twelve hours he had been more drowsy and at times seemed unable to recognize his mother.

Physical examination. He was a well developed, emaciated, stuporous male child of eight years who appeared acutely ill. There was practically no subcutaneous tissue. The skin was sallow and yellowish in color. The sclerae were blue. The right pupil extended upward through the iris. The left was oval in shape. There was a spontaneous horizontal nystagmus of both eyes, more marked on looking to the right, with slow phase to right. There was a dry crusted discharge in both nares. The breath was fetid. There was only a slight suggestion of stiffness of the neck. There was a question of left facial weakness, more marked in the lower face. The tongue protruded to the left. The fundi showed questionable primary atrophy on the right. The left fundus was not well seen. The submaxillary glands were palpable. The chest appeared flat. The breathing was shallow, irregular and almost entirely diaphragmatic. The heart and lungs were negative. The abdomen was markedly scaphoid. There was some difficulty in complete extension of the left arm. There was limitation of extreme motion of the left hip joint. The left leg had been in a spica which had just been removed. There was beginning of breakdown of the skin over the sacrum. There was a positive left Babinski, a left Kernig and a poorly sustained left ankle clonus. There was an equivocal right Babinski inconstantly supported by the confirmatory tests, and a suggestive right Kernig. The "tache cérébrale" was marked.

The blood pressure was 150/92. The temperature was 100°, the pulse 80, the respirations 18.

Laboratory studies. The urine was negative. Blood examinations showed a white cell count of 25,000 with 89 per cent polymorphonuclears and a red cell count of 4,800,000. A lumbar puncture showed an initial pressure of 110. Right jugular compression gave a rise to 200 with return to 110. Left jugular compression gave a rise to 150 with return to 80. Ten cubic centimeters of clear colorless fluid was withdrawn. The fluid came very slowly. There were three cells, two lymphocytes and one polymorphonuclear. There were positive Pandy and alcohol tests. The total protein was 103 milligrams, sugar 81 milligrams, colloidal gold curve 2345555555. There was no pellicle after 24 hours. Tuberculin 1:1000 was negative. A

blood Hinton was negative. The non-protein nitrogen was 50 milligrams and the cholesterol 155 milligrams per 100 cubic centimeters blood serum.

X-rays of the chest and skull were negative.

The boy remained comatose. He occasionally moved the right arm or leg, but the left side remained motionless. At three a.m. on the third day the temperature was 101.2°, the pulse 126, the respirations 25. At 3.15 a.m. his respirations were reduced to three per minute and became shallow; a guttural rattle on breathing developed. The pulse was 140 and weak. Stimulants were given without improving the condition of the patient. Soon respiration ceased altogether. Artificial respiration was unsuccessful, and five minutes later the heart stopped.

Clinical Discussion

Dr. Moriarty: The orthopedic diagnosis was probable Legg Perthe's disease, although the possibility of a tuberculous hip was considered.

Dr. Harold L. Higgins: This was a child who showed trouble with his hip and later showed mental symptoms. One's first thought is tuberculous meningitis. That was pretty well ruled out by the spinal fluid. One would feel that there would be an increase in cells and the formation of a pellicle if this were an out and out tuberculous meningitis.

The question of tuberculoma might be raised, tuberculoma which being near the meninges led to the exudation of a certain amount of globulin; and that was considered. Very much against a tuberculoma, however, was the fact that he had a negative tuberculin test.

The question of syphilis might be considered, probably syphilis of the central nervous system, but the serological tests are quite against it.

It seemed to us when we examined the child first that what had been diagnosed as Legg Perthe's disease, or possibly tuberculous hip, was probably not infection of the hip at all but an early manifestation of a hemiplegia, the hemiplegia becoming more marked on the second episode. With a left hemiplegia one naturally would think of an embolus to the brain, of a cerebral thrombosis, or of a cerebral hemorrhage. There was no particular indication of hemorrhage, as seen by the absence of blood in the spinal fluid. There was no focus found for embolus. The heart was normal. Thus it seemed to me that probably the hemiplegia was to be explained best on the basis of a cerebral thrombosis, and that there is still evidence to be weighed that it might be a brain abscess and not very near the surface of the brain but near enough to cause some changes in the spinal fluid. It might also have been another type of tumor than a tuberculoma, similarly giving signs in the spinal fluid.

The child had a congenital abnormality of his eyes. It was a familial thing. Both he and his brother showed a congenital dislocation of the lens. The child was mentally retarded from apparently what is not to be explained on the basis of anything that happened during life. It was either congenital or something that happened at birth that would explain his mental retardation. It occurred to me that with the presence of a congenital anomaly of the eye there might also be a congenital anomaly of the brain.

Dr. G. Colket Caner: When I saw this child in consultation the tentative diagnosis was tuberculous meningitis. The spinal fluid findings, however, made that diagnosis very unlikely and at the time I saw him made me think of the possibility of brain abscess.

In reviewing the case at present, however, I feel that the diagnosis of brain abscess does not fit the clinical picture very well and that the spinal fluid findings of few cells and a high protein is not usual in brain abscess.

I think the rapidity of the onset should have suggested more strongly the possibility of a vascular etiology. Of course his age was against anything but an embolism and the normal heart findings made that unlikely.

Perhaps the presence of some congenital anomalies should have made us suspect the possibility of others.

Dr. Tracy B. Mallory: What was the boy's race?

Dr. Moriarty: His name is Irish.

Dr. Mallory: I wonder if anyone else would hazard a suggestion as to diagnosis.

A Physician: I wonder how abrupt the onset was. When he began to vomit was it without warning?

Dr. Moriarty: The onset of the vomiting was abrupt. The first appearance of the limp was in July, but the onset of the vomiting was three or four days before the child was admitted to the hospital.

The blood pressure was 150/92. Possibly we should have paid more attention to that.

Dr. James B. Ayer: In connection with that, what is the high limit of non-protein nitrogen in children of this age? Is fifty pretty high? Can you tell me the relation between the time of the lumbar puncture and death?

Dr. Moriarty: The child had the lumbar puncture on the afternoon of admission, two days before death.

Dr. Ayer: It seems as if the lumbar puncture had something to do with it, in your opinion?

Dr. Moriarty: No, I think not.

Dr. Aubrey O. Hampton: Did the blue sclerae suggest fragilitas ossium to you?

Dr. Moriarty: I think not.

Dr. Hampton: How blue do the sclerae have to be before you are sure of that?

Dr. Higgins: My general impression is that you can get blue sclerae without fragilitas ossium. Even with fragilitas ossium you may not have blue sclerae.

DR. MORIARTY: I think the reason they were remarked upon was that the skin was yellow and the sclerae were not.

CLINICAL DIAGNOSES

Tuberculous meningitis?
Brain abscess?

ANATOMIC DIAGNOSES

Arteriosclerosis of the internal carotids.
Cerebral infarct.
Xanthomatosis of the choroid plexus.
Bronchopneumonia.
Lymphoid hyperplasia of the stomach mucosa.
Congenital diminution of the angle between the neck and the shaft of the femur (coxa vara).

PATHOLOGIC DISCUSSION

DR. MALLORY: The autopsy findings on this child are very unusual and I think do not explain any of his symptoms satisfactorily.

In the body, outside the cranial cavity, we found essentially nothing. The hip in which there had been some difficulty in motion and where the x-ray showed some abnormality was abnormal in that the angle of the neck to the shaft was approximately a right angle. On the other hand the structure of the bone cortex was perfectly good. There was no evidence of any old inflammatory process of any sort. It seemed to be an absolutely normal bone except for the rather marked variation from the normal angle. If there had been a pathologic process there it must have been several years ago so that there had been time for absolutely complete repair. The bone was of normal density too, so I think we can rule out abnormal fragility of the bone.

DR. HAMPTON: There was no epiphyseal line in the center of the neck of the femur such as is seen in congenital coxa vara?

DR. MALLORY: No. Except for that angle it was an absolutely normal bone.

There was no nephritis. There was just the least trace of terminal bronchopneumonia.

In the brain there were several abnormal findings about which Dr. Kubik will tell us.

DR. CHARLES S. KUBIK: A large part of the right cerebral hemisphere was soft. The softening, which was pale and not at all discolored, involved the portions supplied by the posterior and middle cerebral arteries, while the part supplied by the anterior cerebral artery was not affected. Both of the internal carotids had very thick walls. The right was almost, if not quite completely, occluded by an old organized process and the greater part of the right half of the arterial circle contained what appeared to be a recently formed thrombus. The situation apparently came about in this fashion: There was unquestionably long standing occlusion of the right internal carotid, but with an intact circle of Willis an adequate supply of blood was obtained by both hemispheres from the basilar and left internal carotid arteries. Then as a terminal event thrombosis in the right half of the arterial circle blocked off the right posterior and middle cerebral arteries while the anterior cerebral artery was supplied from the left side through the anterior communicating artery.

There is another finding which, so far as I know, is not related to the vascular lesions. On the choroid plexus of the lateral ventricles are small whitish nodules. Microscopic examination of these reveals xanthomatosis.

DR. MALLORY: This section is from the internal carotid. Inside the inner elastic membrane there is a very marked intimal thickening which could be the end result of an inflammatory endarteritis or of a simple sclerotic process such as one sees in elderly people. There is at the present time no trace of any progressive inflammation, although the possibility of real endarteritis in the past cannot be ruled out.

Another section with the ordinary eosin methylene blue stain shows a thickened intima and absence of the lymphocytic round cell infiltration which one would expect with a progressive inflammatory lesion.

One of the smaller arteries shown here is almost completely occluded except for a very small canalizing vessel.

This section is from the choroid plexus. Here is one of those little localized areas which Dr. Kubik noted in the gross. Under the microscope it is obvious that it consists of very large pale cells with a foamy cytoplasm, a typical xanthoma. The lesions are multiple.

The difficulty in the case consists in trying to explain why a boy of eight should have a completely occluded carotid artery looking like a process one might expect to find in a very elderly man. One also wonders whether or not these multiple xanthomas have any significance in the case or not. The case does not fit into the clinical picture of any of the three syndromes of multiple xanthomatosis that are recognized. In a child as young as this Niemann-Pick's disease would be most likely. That is almost entirely limited to the Jewish race, and xanthomatous deposits are found throughout the body as well as in the brain.

Have you any further comment, Dr. Kubik?

DR. KUBIK: One thing that may not be very well explained is the fact that there was a gradual onset of hemiparesis over a rather long period of time. Here at autopsy we find what appears to be comparatively recent infarction. The tissue has not even broken down. The landmarks are quite distinct. What caused the early hemiparesis? Is it to be explained by defective blood supply due to partial obstruction in the circle of Willis and finally occlusion with the result we have observed?

DR. CANER: I remember now that he had an

Oppenheim and a Shattuck on the right. Was there any pathologic cause for that?

DR. KUBIK: We did not find any.

DR. CANER: Another question is why he had the high blood pressure if the rest of his arteries were not affected.

DR. MALLORY: They were not in the least. The kidneys and the rest of the body were negative.

DR. CANER: Is that a compensatory thing?

DR. MALLORY: There was no evidence of increased intracranial pressure.

DR. CANER: He had symptoms that somewhat suggested it. The spinal fluid was normal, the blood pressure was 150/90.

DR. MALLORY: I have recently been impressed with the sensitivity of Dr. Hinton's latest modification of his test in presumptive congenital syphilis. Subsequent to our adoption of this method I had found four cases with a positive Hinton reaction, a negative Wassermann and absolutely negative clinical signs. These were all brought into the hospital because someone else in the family had been found to have a positive Wassermann. In each family there had been miscarriages, then finally an apparently normal child with a negative Wassermann but a positive Hinton. I think this last Hinton test is sensitive enough to pick up some cases of congenital syphilis that would never have been suspected by the other method. Whether that is true in this case I am not prepared to say.

DR. AYER: We do see cases that are undoubtedly congenital syphilis, with a negative Wassermann.

DR. MORIARTY: This was a Hinton.

DR. MALLORY: Yes, but not the most recent modification. There has been a sharp increase in sensitivity since we shifted to the last modification.

Did we have a Wassermann report on the spinal fluid?

DR. MORIARTY: It could not be done. There was not sufficient fluid.

CASE 19472

CAN UNCOMPLICATED EMPHYSEMA CAUSE SUDDEN DEATH?

PRESENTATION OF CASE

DR. F. DENNETTE ADAMS: This is the case of a private patient, a single white man of sixty-seven who was admitted to the hospital on January 27, 1933 because of severe dyspnea, weakness and loss of weight.

The past history was irrelevant. There had been no serious illnesses.

Ten or twelve years previously he had begun to notice gradually increasing but not severe shortness of breath on exertion. He had seen several physicians but a definite diagnosis had not been made until 1926, when he was sixty-one. He was at that time examined by Dr. L. B. Morrison, a roentgenologist, who established a diagnosis of emphysema and expressed the opinion that the pulmonary changes demonstrated by x-ray were sufficient to account for the symptoms.

I saw him for the first time a year later and followed him until his death in 1933. During these six years dyspnea increased gradually but definitely. At first it was present only on stair climbing, fairly rapid walking or some other comparable exertion. There was no orthopnea. Two years later he was decidedly short of breath on walking slowly up five or six stairs and was unable to walk more than a hundred yards without extreme discomfort. There was also gradual loss of strength.

Physical examination was always essentially negative except for a moderate degree of arteriosclerosis and the lung findings. Dyspnea and cyanosis appeared with activity but were not present with the patient at rest. The lungs were hyperresonant throughout, more at the right base. The breath sounds were of the type commonly associated with emphysema with the exception of the lower half of the right lung posteriorly, where breath sounds were practically absent. Apparently in this region the lung did not expand and contract sufficiently to produce readily audible sounds.

By 1930 the patient had reached the point where the slightest exertion, such as walking only a few yards, produced dyspnea and cyanosis and he was incapable of any but the slightest physical activity. At this time Dr. Morrison x-rayed him again and reported as follows: "This is the most marked case of emphysema I have ever seen." For the last three years of his life the patient was confined to the house. Each year he was kept in bed at the hospital for a month in an effort to increase his reserve. After such a period of prolonged rest there was slight improvement, but this was always temporary. He was discharged from the hospital in April 1932, and was seen only once between then and the time of his final admission on January 27, 1933.

During this period of nine months he had left his room on only two occasions because his dyspnea made it impossible for him to accomplish any physical activity. Although his dining room was on the same floor as his bedroom and a scant hundred feet away, he had had all meals served in his room because of the discomfort attendant upon getting as far as the dining room. On physical examination there were now dyspnea and cyanosis even at rest. Orthopnea was not pronounced. The lungs seemed to move even less than previously, breath sounds being faint throughout and hyperresonance being marked. There was no evidence of any cardiac disorder. He was fully as comfortable lying down as he was sitting up. He was kept constantly in bed, but the dyspnea, cyanosis and

weakness continued to increase. There had been gradual loss of weight during the final year. He died on February 28, 1933, thirty-two days after admission to the hospital.

Dyspnea, cyanosis and weakness were profound during the final weeks of the illness and all were apparently due to inability to obtain sufficient oxygen. Oxygen inhalation in the final stages of the illness provided some increase in comfort but very little change in the character of the breathing or the cyanosis. There was at no time evidence of cardiac failure or of terminal infection. His death was unusual by virtue of absence of any change in signs. There was no marked increase in dyspnea and no change in cardiac situation such as we so often see shortly prior to demise. I saw this patient on the final day of his illness at seven p.m. He seemed to be in exactly the same condition as he had been for the two or three days previously. Ten minutes later he simply stopped breathing.

Clinical Discussion

Dr. Adams: There was at no time anything in the history or physical examination of this man to justify a diagnosis other than emphysema and arteriosclerosis and unless one can establish some relationship between these two conditions then it can be said that the arteriosclerosis was an incidental factor. In other words, he did not die of arteriosclerotic heart disease with failure. As already indicated, there was no evidence of terminal infection which one so often sees in cases of emphysema. He is the only patient I recall having seen in whom I felt certain that the remote cause of death and the immediate cause as well was emphysema.

Dr. Aubrey O. Hampton: This film was taken about three years before death. The diaphragm is at the twelfth rib on both sides. It is lower on the right than on the left. The right lung is much more radiant than the left, particularly in the upper half. More blood vessels are visible on the left than on the right, and they are closer together. These are very clear, sharply defined lines as though they were the outlines of large blebs. I do not see any blood vessels at all along the axillary line.

The heart is displaced towards the left side. It is small. The aorta is tortuous. I do not see anything abnormal in the gastro-intestinal examination.

Dr. Adams: The gastro-intestinal examination was a precautionary measure in this case. The patient had occasional nausea and epigastric distress, and during one of his earlier admissions we had the roentgenological studies in order to exclude the possibility of any organic disease of the digestive tract, although there were scant grounds for suspecting any.

Dr. Hampton: In the lateral and oblique views the blebs of emphysema are much more easily seen, I suppose because they are in the anterior lung tips, where they are most common.

Clinical diagnoses (from hospital record)

Emphysema.
Arteriosclerosis.

Anatomic diagnoses

Pulmonary emphysema, senile.
Arteriosclerosis, moderate aortic and coronary.
Acute glomerular nephritis.

Pathologic Discussion

Dr. Tracy B. Mallory: The autopsy confirmed the clinical impression entirely, though the histologic examination added one complete surprise in the form of a terminal, fairly severe acute glomerular nephritis. He had as extreme a grade of emphysema as I have ever seen, and we found nothing else except a moderate degree of arteriosclerosis. I have his right lung here. It has been dried in the inflated position with a constant air stream. At the base, where the specimen has been ruptured a little, one can look in and see the size of some of the air sacs. The biggest are four to six centimeters in diameter. It is interesting that in spite of that extreme change in the right lung the left one, though not quite so bad as that, was nearly as severe.

His heart weighed only 320 grams, which we ordinarily consider a normal weight. I think that probably may represent a slight degree of hypertrophy for him, because he could hardly weigh over one hundred pounds and all his organs were small. His liver, for instance, weighed only 800 grams. But even taking those relative weights into consideration, we still have rather strikingly little cardiac hypertrophy with as extreme a case of emphysema as one ever sees.

Dr. Hampton: How large was the pulmonary artery?

Dr. Mallory: At the level of the valve—I have no measurement beyond it—it was 6.8 centimeters, which is a little smaller than average rather than larger.

Some of you may recently have seen an article by Kountz and Alexander[1] regarding the etiology of emphysema in which they make the claim that rigidity of the spine and the joints of the ribs is essentially the most important etiological factor. It is interesting that in this man the spine was as flexible as it would be in a man of twenty-four. There was absolutely no serious grade of arthritis whatever. The intervertebral disks were quite elastic and one could flex his spine without any trouble at all.

Another theory of the etiology of emphysema is the loss of elastic tissue in the alveolar walls. The elastic tissue stains from this case show more elastic tissue than normal rather than

less. So I do not feel that the case helps us very much in regard to the etiology of emphysema except to show that at least two of the fairly widely accepted theories do not necessarily hold.

DR. ADAMS: May I add in this connection that two years before this patient died I asked Dr. Churchill to see him with reference to the possibility of enlarging the chest surgically. We decided against surgical interference because it seemed likely that his lungs were so dilated that little added function could be obtained even should thoracic space be increased.

DR. MALLORY: Of course the intrathoracic volume is already considerably above normal in most of these people. In fact Loeschke[2] makes out an excellent case for believing this to be the primary difficulty.

A PHYSICIAN: Is there any explanation as to why some cases of emphysema have cardiac failure and others do not?

DR. MALLORY: No, I do not know of any accepted one. Three explanations have been suggested, one that cases of pulmonary emphysema have a very marked degree of pulmonary arteriosclerosis. That is usually true. This man had a considerable amount but he did not have cardiac hypertrophy. Another suggestion is that the actual number of pulmonary capillaries is tremendously diminished, so that the capillary space through which the blood must be forced is only one-third to one-fourth of normal. Finally there is much suggestive evidence but no rigid proof that inflation and deflation mechanically aid the distribution of blood throughout the lung. When respiratory movements are diminished by either collapse or emphysema, increased force is required to force the blood along[3, 4].

DR. ADAMS: What may be called the immediate cause of death was always a puzzle to me in this man. Of course during the last week of his illness he was extremely weak. I saw him one night about six o'clock and as far as I could tell his condition was just as it had been, no elevation of pulse and no marked increase in respirations. I decided that he was somewhat weaker, otherwise in just the same condition. I left the Phillips House, and when I got home I received the telephone message that he had died.

DR. WYMAN RICHARDSON: Another possible explanation for the failure of the heart is that suggested by Professor Rist in his lecture at this hospital last year. He believes that it cannot contract efficiently because of the inelasticity of the emphysematous lung. It may have acted exactly like massive fibrosis of the lungs.

DR. MALLORY: I had for the moment forgotten Professor Rist's lecture. That too is a logical possibility. Loeschke, however, in measurements of the elasticity of emphysematous lungs found as a rule no loss of elasticity.

REFERENCES

1 Kountz, W. B., and Alexander, H. L.: Nonobstructive emphysema. J. A. M. A. 1933, 100:551.
2 Loeschke, H.: Handb. d. spez. path. Anat. u. Histol. Henke, F. u. Lubarsch, O. Springer, Julius, Berlin. Vol. III, Part I, p. 612.
3 Heinbecker, Peter: Am. J. Physiol. 1927, 81:170.
4 Cloetta: Arch. f. exper. Pathol. u. Pharmakol. 1912, 70:407.

The New England
Journal of Medicine

SUCCESSOR TO
THE BOSTON MEDICAL AND SURGICAL JOURNAL

Established in 1828

Published by THE MASSACHUSETTS MEDICAL SOCIETY under the jurisdiction of the

COMMITTEE ON PUBLICATIONS

R. I. LEE, M.D., *Chairman* HOMER GAGE, M.D.
R. B. OSGOOD, M.D. R. M. SMITH, M.D.
F. H. LAHEY, M.D.

EDITORIAL STAFF

REID HUNT, M.D. STEPHEN RUSHMORE, M.D.
JOHN P. SUTHERLAND, M.D. HANS ZINSSER, M.D.
GEORGE R. MINOT, M.D. BENJAMIN WHITE, PH.D.
FRANK H. LAHEY, M.D. HENRY R. VIETS, M.D.
SHIELDS WARREN, M.D. ROBERT N. NYE, M.D.
GEORGE L. TOBEY, JR., M.D. ROBERT M. GREEN, M.D.
C. GUY LANE, M.D. CHARLES C. LUND, M.D.
WILLIAM A. ROGERS, M.D.

WALTER P. BOWERS, M.D., *Managing Editor*

ASSOCIATE EDITORS

GEORGE G. SMITH, M.D. WILLIAM B. BREED, M.D.
JOSEPH GARLAND, M.D.

THE NEW HAMPSHIRE MEDICAL SOCIETY
PUBLICATION COMMITTEE

D. E. SULLIVAN, M.D. BENJAMIN P. BURPEE, M.D.
LAWRENCE HAZZARD, M.D.

THE VERMONT STATE MEDICAL SOCIETY
PUBLICATION COMMITTEE

WILLIAM G. RICKER, M.D. C. F. DALTON, M.D.
E. A. STANLEY, M.D.

SUBSCRIPTION TERMS: *$6.00 per year in advance, postage paid for the United States, Canada $7.04 per year, $8.52 per year for all foreign countries belonging to the Postal Union.*

Material for early publication should be received not later than noon on Saturday. Orders for reprints must be sent to the Journal office, 8 The Fenway.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to The New England Journal of Medicine, 8 The Fenway, Boston, Mass.

AMOEBIC DYSENTERY

THE public press has recently contained important news items of an epidemic of amoebic dysentery traceable to carriers in a Chicago hotel. The latest report from Dr. Herman Bundesen, President of the Chicago Board of Health, is that 180 cases and 19 deaths have occurred. A report on the situation appeared in the *Journal of the American Medical Association*, November 18, 1933. It is learned, however, from a Boston physician who has been coöperating in the study of this epidemic that a most serious feature of it is due to the wide scattering of many of the patients before the onset of their symptoms and of the missing of the diagnosis by many excellent practitioners who did not happen to be familiar with this disease in an acute form. Equally important is the fact that negative reports on stool examinations for amoebae cannot be trusted to rule out the disease. Several cases have had the diagnosis made only at autopsy, previous search for the endamoeba histolytica having been fruitless. The symptoms of this disease are very variable, and some of the patients have been operated on for supposed acute appendicitis, cancer of the intestine and other diseases. Surgery is very harmful in such cases. The lesson to be learned is that in any case of acute colitis a therapeutic test with emetine, Gm. 0.065 orally or subcutaneously once a day for six to ten days must be given whether the amoebae are found in the stool or not. This drug is dangerous if given too long. If the case, however, is amoebic, results will be shown in less than ten days and may be shown in twenty-four hours.

The reason the cases have been missed is, of course, their apparent rarity in Northern United States. Last year in Massachusetts there were only four cases of amoebic dysentery reported and two deaths. Of course there were probably more cases than have been recognized.

In view of the Chicago epidemic there is reason to believe that other similar epidemics may occur elsewhere unless there is more strict bacteriological control of persons handling food than heretofore.

Doctors throughout the country should view with suspicion the illness of persons who visited Chicago this summer or fall.

An appeal for careful study of unusual disturbances of the gastro-intestinal tract by Dr. Henry D. Chadwick, State Commissioner of Public Health, is especially significant at this time and appears on page 1070 of this issue.

THE MILK CODE AND THE HOSPITALS

THE one thing that the new Federal milk code does more successfully than anything else is to swell the profits of the dealers at the expense of the consumers without appreciable profit to the farmer. The protest against this shrewdly framed code has not as yet borne fruit and only through aroused public opinion can the gross unfairness be reformed. Before the code, hospitals were paying 7¾ cents a quart for milk and the farmer was receiving 6¼ cents a quart, assuming he was fortunate enough to have to sell no milk as "surplus". Under the code, hospitals must pay 9¼ cents a quart (smaller hospitals even more), and the farmer gets only 6½ cents—again for milk not rated as "surplus". Actually the farmer may average little better than 3½ cents a quart. Who gets the difference? For whose benefit was this code framed? A series of revealing articles on the milk situation, now appearing in the *Boston Herald*, presents the whole picture more clearly. Milk dealers were glad to get the business of the hospitals at 7¾ cents a quart—what justification is there for the new price?

The hospitals are not profit-making institutions. They are charitable institutions and their

funds are devoted to the care and cure of the sick and injured who come to them for help. If money must be spent for exorbitantly priced milk, if the present code is allowed to stand, the hospitals will have just so much less money to care for their sick. All will agree that the farmer deserves a fair price for his product and the dealer a fair price for its handling and distribution, but the present plan smells strongly of profiteering, profiteering of the meanest type at the expense of the sick and the injured poor of the community.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

McKITTRICK, LELAND S. B.S., M.D. Harvard University Medical School 1919. F.A.C.S. Surgeon-in-Chief, Palmer Memorial Hospital. Surgeon, New England Deaconess Hospital. Assistant Visiting Surgeon, Massachusetts General Hospital. Instructor in Surgery, Harvard. His subject is "Abdominal Symptoms with or without Abdominal Lesions in Diabetic Acidosis." Page 1033. Address: 205 Beacon Street, Boston.

FITZ, REGINALD. M.D. Harvard University Medical School 1909. Associate Professor of Medicine, Harvard Medical School. Physician to Peter Bent Brigham Hospital, Boston. His subject is "Diseases of the Biliary Tract. Diagnosis and Treatment. Medical Aspect." Page 1037. Address: 721 Huntington Avenue, Boston.

HOLMES, GEORGE W. M.D. Tufts College Medical School 1906. Roentgenologist, Massachusetts General Hospital. Clinical Professor of Roentgenology, Harvard Medical School. His subject is "The Roentgen Examination of the Gall Bladder." Page 1039. Address: 265 Charles Street, Boston.

BAZIN, A. T. M.D., C.M. McGill University Faculty of Medicine 1894. F.A.C.S. Professor of Surgery, McGill University. Attending Surgeon, Montreal General Hospital. His subject is "Surgical Aspect of Diseases of the Biliary Tract." Page 1042. Address: 4064 Dorchester Street, West, Montreal, Canada.

BYRNE, HARRY V. M.D. Tufts College Medical School 1929. Assistant Surgeon in Ophthalmology, Boston City Hospital 1933-. Assistant Laryngologist, Long Island Hospital 1933-. His subject is "The Use of Benzyl-Methyl-Carbinamine-Carbonate in the Treatment of Rhinitis." Page 1048. Address: 371 Commonwealth Avenue, Boston.

FITZHUGH, GREENE. M.D. Harvard University Medical School 1927. Assistant in Medicine, Massachusetts General Hospital, and Courses for Graduates, Harvard Medical School. His subject is "Agranulocytosis." Page 1051. Address: 12 Hereford Street, Boston.

DAMESHEK, WILLIAM. M.D. Harvard University Medical School 1923. Associate Physician, Beth Israel Hospital, Boston. Physician, Boston Dispensary. Physician to the Blood Clinics of the Beth Israel Hospital and Boston Dispensary. Instructor in Medicine, Tufts College Medical School. His subject is "Agranulocytosis. Report of Three Cases Treated with Nucleic Acid Derivatives." Page 1054. Address: 371 Commonwealth Avenue, Boston.

CHRISTIE, WELMAN B. M.D. Boston University School of Medicine 1927. Second Assistant Visiting Surgeon, Massachusetts Memorial Hospitals, Boston. Assistant to the Gynecological Out Patient Department, Massachusetts Memorial Hospitals. Assistant in Gynecology and Anatomy, Boston University School of Medicine. His subject is "Needle Holder for Blood Transfusion and Intravenous Therapy." Page 1062. Address: 15 Bay State Road, Boston.

THE OUTBREAK OF AMOEBIC DYSENTERY IN CHICAGO

The Commonwealth of Massachusetts
Department of Public Health
State House, Boston

November 17, 1933.

Editor, *New England Journal of Medicine,*

I have received the following telegram from Dr. Herman N. Bundesen, Commissioner of Health of Chicago:

> "An outbreak of amoebic dysentery has been uncovered by us in several hotels and eating places in Chicago. We have records of guests that have carried the infection to many points throughout the country. These cases are not generally recognized as amoebic dysentery and some of them have been operated upon for appendicitis or ulcerative colitis with unfortunate results. At the suggestion of Doctor Spencer who is representing the U.S.P.H.S. and coöperating with us in this study, we are asking you to inform the physicians and local health officers of your State to be on the alert for such cases and if you find any that have had their origin in Chicago will you kindly wire me collect so that we may complete our records."

We have just had reported to us four cases of amoebic dysentery in Beverly and one case in Worcester. The diagnosis in these cases has been confirmed by laboratory tests. The pa-

tients all attended the convention of the American Legion in Chicago. We have sent out the following letter to Post Commanders of the American Legion:

> "Cases of amoebic dysentery have appeared among Legionnaires who attended the recent convention in Chicago. Although the cases so far recognized in Massachusetts have not been serious, there is considerable evidence that many of those at the convention may have had relatively mild attacks following their return. Unless proper precautions are taken these may in turn infect other members of their families. May we request that you notify all members of your Post who attended the convention that they may have been exposed to this infection and that if any of them have had intestinal disorders since their return, they should consult their family physicians.
>
> "The Department would greatly appreciate any information that you can furnish as to such conditions within the membership of your Post, and especially the names of those engaged in food handling occupations who attended the convention."

Because of the large number of persons from Massachusetts other than Legionnaires who have been in Chicago during the fall to attend the World's Fair, it is desirable that physicians be notified of the possibility of amoebic dysentery being found at this time. Our records show that cases of amoebic dysentery have occasionally been found in Massachusetts. In 1928 there were 11 cases, largely among the sailors at the Marine Hospital; in 1929, 1 case; in 1931, 5 cases; in 1932, 4 cases; in 1933, 4 cases.

This being such an unusual disease in this State, physicians will not be familiar with the treatment. I would suggest that you get a statement from Dr. Strong, giving details as to treatment and publish it with this letter.

Yours truly,
HENRY D. CHADWICK, M.D.,
Commissioner of Public Health.

THE TREATMENT OF AMOEBIC DYSENTERY

BY RICHARD P. STRONG, M.D.

THE treatment of amoebic dysentery should receive careful supervision. During the acute stages of the disease the patient should be kept in bed. In the cases with numerous bowel movements, only liquid diet should be allowed. In general the diet should be carefully regulated according to the frequency and character of the bowel movements, and in all cases should be bland.

Emetine is the standard drug for specific treatment. It should be given during the acute stages of the disease in doses (for adults) of one grain of emetine hydrochloride dissolved in 1 cc. of distilled water, either by hypodermic or intramuscular injection, this dose being continued for a week to 10 days, or even 12 days, if special susceptibility to the drug is not manifested. Such treatment in a number of cases does not cause complete eradication of the infection, and if amoebae are still present in the dejecta it should be supplemented by a second course of treatment with the double iodide of emetine and bismuth (emetine bismuth iodide), containing about 26% of emetine. Three-grain doses of this preparation should be given by the mouth for 10 or 12 consecutive days. This drug is almost insoluble in neutral or acid solutions, but dissolves readily in the alkaline contents of the intestine.

Although it is only slightly soluble in the gastric contents, some nausea and even vomiting sometimes follows its administration. It therefore is best given in powdered form in gelatin capsules. On account of its irritating action in the stomach, it is often desirable to give the dose at bed time, and advise the patient to take no food for three or four hours before the medicine. After its administration he should remain absolutely at rest in bed.

A number of pharmaceutical preparations have been made with the object of reducing the nauseating and emetic effect of emetine and at the same time retaining its therapeutic action. However, the evidence is not conclusive that the use of such preparations gives as favorable results as do the drugs already referred to.

Recently Willmore and Martindale have recommended for use Auremetin, the hydrogen periodide of emetine in combination with the dye auramine. This drug was said to give rise to no nausea or vomiting. The dose recommended was one grain given in soft gelatin capsules four times daily on alternate days for a week, and then daily till a total of 40 to 60 grains is ingested. Philip W. Brown (1929) found that such doses cause nausea, and usually vomiting, and he had to decrease the dose to 2 grains daily.

The physician should bear in mind that emetine is poisonous, and that there may be cumulative action of the drug which may manifest itself in asthenia and polyneuritis and cardiac complications. Also, the margin between the toxic and therapeutic dose of emetine is small, therefore for patients in whom the symptoms do not yield to treatment in a week or ten days the drug should be interrupted for a short period before a second course of treatment is instituted.

In the cases of peripheral neuritis occurring after treatment with emetine, the symptoms are

usually manifested by general muscular pains and weakness, especially in the legs, progressing sometimes to paresis. Wrist-drop and toe-drop may occur. These symptoms, however, usually disappear gradually with the stopping of emetine. In twenty cases of poisoning from the use of emetine collected from the literature, in six of these less than 10 grains were given. All recovered except one case who received daily subcutaneous injections of one and one-half grains of emetine hydrochloride for 20 days, a total of 29 grains. Diarrhea also may be an important symptom of emetine poisoning. Rogers believes that 15 grains of emetine usually constitutes a fatal dose for an adult man.

Many cases of amoebic dysentery, particularly those with advanced lesions, do not yield to treatment with emetine, and relapses after the use of the drug are not very uncommon. It is especially active in destroying the vegetative forms of the amoebae. Whether it precipitates encystation or not, it is evidently not so effective in destroying or rendering the stools free of the amoebic cysts. Although the cysts probably do not ex-cyst in the bowel, the patient may be at least theoretically a locus of infection. It therefore is of extreme importance that the cases of amoebic dysentery should be treated early, and that symptoms of relapse should have prompt and careful attention.

A number of arsenical preparations have been employed in the treatment of the disease. Stovarsol (acetylaminohydroxyphenylarsenic acid) in four grain doses, twice daily, for a course of a week at a time, in the hands of some observers, has acted beneficially in checking the diarrhoea in the chronic cases.

Brown believes that Treparsol (formyl amide of meta-amino-para-oxyphenyl-arsenic acid) is less toxic and more rapidly eliminated than Stovarsol, and is therefore preferable. He recommended 0.75 gram of this drug daily for four days. This amount contains approximately 800 milligrams of arsenic.

Treatment with these drugs must be carefully watched, as toxic erythema or even an arsenical exfolliative dermatitis may ensue.

Another preparation, Acetarsone (acetylaminohydroxyphenylarsonic acid) has been recommended particularly by Craig (1929) for the treatment of chronic or latent infections. This preparation contains approximately 27 per cent of arsenic. It should be given by the mouth in compressed tablets containing 0.25 gram. Craig recommends one-half tablet three times a day for one week, with cessation of the treatment for one week, and then one-half tablet three times a day for one week longer. He states that in most of his cases this dosage has been found sufficient to cause the disappearance of the parasite, but in some cases it has been found necessary to repeat the course of treatment. He has seen but two cases of severe poisoning from such treatment.

Finally, Anderson (1932), David, Johnstone, and Stanley (1932), have recommended oral treatment with Carbarsone (4-carbaminophenylarsonic acid) containing 28.8 per cent arsenic. Anderson recommends a dosage of one capsule, 0.25 gram, twice daily for 10 days, a total of five grams. No toxic effects were noted, though David, Johnstone, and Stanley remark that the dose of five grams in 10 days may not be sufficient to cure severe cases of amoebiasis.

Iodine in the form of iodine-oxyquinolin-sulphonic acid ("Yatren") has also been extensively employed in the past few years in the treatment of amoebic dysentery. This preparation can be given by the mouth, by enema, or subcutaneously. The dose recommended is one gram (15 grains) in powdered form in capsules, three times a day for 10 days, and after an interval of one week the course should be repeated. Manson-Bahr believes that in order to obtain permanent results Yatren must be given by the rectum in the form of rectal injection of a 2.5 per cent solution of the drug in warm water, as well as by the mouth. The course of injections is continued when well tolerated for 10 days. Sometimes a longer period may be necessary. He believes that strict dieting and rest in bed are absolutely necessary while the treatment is being pursued.

Anayodin, in which 22 per cent of sodium bicarbonate is added to the iodine oxyquinoline sulphonic acid, is similar in its effects to Yatren. The sodium bicarbonate is added to increase the solubility of the drug but not for any therapeutic action. O'Connor (1932) and Neumann (1932) have both reported good results in the treatment with Anayodin.

Biggam, Halawani and Ragab (1931) have studied the effects of treatment with Yatren in Cairo, employing pills containing 0.25 gram of Yatren. Two pills t.i.d. failed to bring about any definite improvement. Three pills t.i.d. for the same period of time gave beneficial results, but the best results were obtained by four pills t.i.d. for 15 consecutive days. Of 37 patients treated by the last method, no curative effects were observed in two, and the parasites persisted. Satisfactory tests to determine the permanence of cure could be carried out only in 18 of the 37 cases. Of these, 13 (72.2%) were found to be apparent cures; five were failures.

Sellards has found that the plant Castela nicholsoni contains an active principle, probably a glucoside, which is valuable in the treatment of amoebic dysentery, but reliable preparations of this plant are not available commercially.

As an adjuvant to emetine treatment, tablets of "Kurchee" bark (*Holarrhena antidysenterica*) which contains conessine, in 10 grain doses, two or three times a day, have also been

recommended especially in India by Acton and Chopra (1933) and Ghosh (1933).

Deeks, O'Connor, and James in Panama have also advocated bismuth subnitrate in heroic doses, especially as an adjuvant to emetine treatment.

Treatment of Carriers. The cysts of *Entamoeba histolytica* are not infrequently found in the feces of healthy individuals. Where proper disposal of human feces is carried out, the individual who harbors cysts in the intestine cannot usually be regarded as a menace, and hence prolonged treatment of him from the standpoint of public prophylaxis is hardly justifiable.

Craig (1929) has found that many cases of latent amoebic infection suffer with symptoms which are often indefinite, but usually confined to the digestive and nervous systems. However, as the writer has reported elsewhere, in other instances such infections have been known to exist over long periods without the slightest symptoms, and individuals known to be carriers during life who have succumbed to other diseases, have shown no gross lesion of the intestine at autopsy.

Milam and Meleney (1931), in an intensive study of a rural community in Tennessee, have found no correlation between the occurrence of dysentery and the harboring of *Entamoeba histolytica.* Other symptoms, possibly referable to amoebiasis, were found to be as common among non-carriers as among carriers of *Entamoeba histolytica.* They concluded that their findings indicated that the mere presence of cysts did not warrant special public health measures to bring about the immediate reduction of this possible source of infection.

The cysts of *Entamoeba histolytica* often continue to be passed in the stools, and are not destroyed by any known method of treatment. In a large series of cases of amoebic infections, some are always found to be refractory to treatment. Hence, in countries where amoebic dysentery does not prevail, it would seem to be more advisable to continue to observe such individuals rather than submit them to frequent treatment. Obviously, in no case should a cyst-carrier be employed in the preparation or handling of food, or cleaning or filling drinking water receptacles. The cysts of *Entamoeba histolytica* cannot withstand desiccation.

David, Reed, and Leake have recently used vioform N. N. R. (iodochloroxyquinoline) similar in its action to Yatren and Chiniofon. The use of this preparation must still be regarded as in the experimental stage.

REFERENCES

Acton, H. W., and Chopra, R. N.: Indian Med. Gaz., Jan. 1933, vol. 68, No. 1, p. 6.
Anderson, H. H.: Am. J. Trop. Med., Nov. 1932, vol. 12, No. 6, p. 459.
Biggam, A. G., Halawani, A., and Ragab, A.: Tr. Royal Soc. Trop. Med. & Hyg., Nov. 30, 1931, vol. 25, No. 3, p. 209.
Brown, P. W.: Ann. Int. Med., 1928-29, vol. 2, p. 177.
Craig, C. F.: International Clinics, March 1929, vol. 1, p. 77.
David, N., Johnstone, H., and Stanley, L. L.: Am. J. Med. Sci., 1932, vol. 184, p. 716.
David, Reed, and Leake: Jour. A. M. A., Nov. 18, 1933, vol. 101, p. 1641.
Ghosh, A. B.: Indian Med. Gaz., Jan. 1933, vol. 68, No. 1, p. 13.
Milam, D. F., and Meleney, H. E.: Am. J. Hyg., Sept. 1931, vol. 14, No. 2, p. 325.
O'Connor, F. W., and Neumann, E.: Trop. Dis. Bull., Apr. 1932, vol. 29, No. 4, p. 252.
Sellards, A. W.: Cecil's "Text-Book of Medicine", 3d edit., 1933, p. 396.

MISCELLANY

THE FEDERAL EMERGENCY RELIEF ADMINISTRATION

THE PRESIDENT'S LETTER TO THE PRESIDENTS OF DISTRICT MEDICAL SOCIETIES

The Massachusetts Medical Society
8 The Fenway, Boston, Mass.

November 20, 1933.

Dear Doctor:

In many of the cities and towns of Massachusetts, especially those where mills have closed, there is a large number of unemployed persons. Doubtless the physicians of these communities have cared for the sick in this class with little or no remuneration because many of the families left without the means of buying food, coal and clothing have been compelled to subsist upon aid received from welfare organizations. Physicians have given their services to the indigent sick for so long that it has become a tradition but physicians are suffering now with many other classes and it is manifestly fair that they should be paid something for their work. Many have overlooked the fact that the medical profession as a group requires relief in about the same proportion as others.

At a conference with representatives of the Federal and State Emergency Relief Administration on November 16 the problem of furnishing the same type of medical, dental and nursing service to an indigent person as to a private patient was discussed. The Federal Government is particularly anxious to maintain the traditional family and family-physician relationship in the medical care of the indigent sick in their homes and the common aim should be the provision of good medical care at a low cost to the mutual benefit of the indigent patient, physician, dentist and nurse. In some States a precedent has been established whereby a reduction of one-third of the customary fee for office, home and confinement service has been acceptable. As such a plan seems fair may we suggest that you call a committee of three in your district to establish fee-tables on this basis in your various communities.

It should be remembered that such a fee-table is to be designed for the indigent and while not strictly confidential there is no occasion for its publication since its use is to be confined to the present emergency and ceases with the advent of normal times. Therefore care must be taken that a precedent is not established which would be difficult to dissolve when prosperity returns.

Since the Federal and State Governments are ready to render aid in these cases and are expecting action

from the Massachusetts Medical Society, I urge you to take immediate steps in your district to bring the plan to fruition. Please let me hear from you as soon as possible.

A physician who wishes to do relief work must notify his local welfare board at once, as approval by the latter is absolutely necessary in each indigent case.

Very sincerely yours,

WILLIAM H. ROBEY, M.D., *President.*

RULES AND REGULATIONS

No. 7

GOVERNING MEDICAL CARE PROVIDED IN THE HOME TO RECIPIENTS OF UNEMPLOYMENT RELIEF

INTRODUCTION

The conservation and maintenance of the public health is a primary function of our Government. In this emergency, the ingenuity of Federal, State, and local relief officials is being taxed to conserve available public funds and, at the same time, to give adequate relief to those in need. To assist State and local relief administrations in the achievement of these aims, with regard to medical care, two steps have been taken: First, to define the general scope of authorized medical care, where the expenditure of Federal Emergency Relief Funds is involved; and second, to establish general regulations governing the provision of such medical care to recipients of unemployment relief.

GENERAL SCOPE

(Extracted from rules nos. 1 and 3, previously established)

Promulgated on June 23, 1933, rule no. 1, section (b), stated:

> Grants made to the States from Federal funds under the Federal Emergency Relief Act of 1933 may be used for the payment of medical attendance and medical supplies for those families that are receiving relief.

The permission granted under this section (b) was more sharply defined in the same rule, in section (d), which stated in part:

> These funds may not be used for the payment of hospital bills * * *, or for providing general institutional care. These necessary services to the destitute should be made available through State or local funds.

In the section on "Direct Relief" of rule no. 3, promulgated on July 15, 1933, medical care in the home was listed as item 6 in the list of the types of relief that may be provided to relief cases, viz.:

> "6. Orders for medicine, medical supplies and/or medical attendance to be furnished in the home." Under the same rule, adequacy of such relief is made "an obligation on the State Emergency Relief Administration and on all the political subdivisions of the States administering relief * * *."

The scope of medical care as above defined shall be construed to include: Bedside nursing care, as an adjunct to medical care; and emergency dental service for those families that are receiving relief.

REGULATIONS GOVERNING MEDICAL CARE PROVIDED IN THE HOME TO RECIPIENTS OF UNEMPLOYMENT RELIEF

The following regulations, governing the provision in the home of medical care (includes "medicine, medical supplies and/or medical attendance") to persons eligible for unemployment relief, are hereby established.

1. *Policy.*—A uniform policy with regard to the provision of medical, nursing, and dental care for indigent persons in their homes, shall be made the basis of an agreement between the relief administration and the organized medical, nursing, and dental professions, State and/or local. The essence of such a policy should be:

(*a*) An agreement by the relief administration to recognize within legal and economic limitations, the traditional family and family-physician relationship in the authorization of medical care for indigent persons in their homes; the traditional physician-nurse relationship in the authorization of bedside nursing care; the traditional dentist-patient relationship in the authorization of emergency dental care; and

(*b*) An agreement by the physician, nurse (or nursing organization), and dentist to furnish the same type of service to an indigent person as would be rendered to a private patient, but that such authorized service shall be a minimum consistent with good professional judgment, and shall be charged for at an agreed rate which makes due allowance for the conservation of relief funds.

The common aim should be the provision of good medical service at a low cost—to the mutual benefit of indigent patient, physician, nurse, dentist, and taxpayer.

The policy adopted shall be to augment and render more adequate facilities already existing in the community for the provision of medical care by the medical, nursing, and dental professions to indigent persons. It shall imply continuance in the use of hospitals, clinics, and medical, dental, and nursing services already established in the community and paid for, in whole or in part, from local and/or State funds in accordance with local statutes or charter provisions. Federal Emergency Relief Funds shall not be used in lieu of local and/or State funds to pay for these established services.

The phrase "in their homes" shall be interpreted to include office service for ambulatory patients, with the understanding that such office service shall not supplant the services of clinics already provided in the community.

2. *Procedure.*—A uniform procedure for authorization of medical, nursing, and dental care in the home shall be established by each State and/or local emergency relief administration. This procedure shall not be in conflict with the following requirements:

(*a*) *Written order.* — All authorizations for medical, nursing, and dental care shall be issued in writing by the local relief officer, on the regular

relief order blank, prior to giving such care; except that telephone authorization shall immediately be followed by such a written order; and provided that authorizations for bedside nursing care shall be based on a recommendation by the attending physician, in cases where a physician is in attendance, who shall certify to the need for nursing service as part of the medical care. Authorizations for medicine and medical supplies shall also be issued in writing and, in general, such authorizations shall not be issued except upon written request of the physician authorized to attend the person for whose use they are desired.

(*b*) *Acute illness.*—Authorizations for medical care for acute illness shall be limited to a definite period and a maximum expenditure or number of visits (i.e., not more than 2 weeks or 10 visits), according to the standard agreement made between relief officials and physicians under regulation 1. Medical care in excess of this period shall not be authorized until after a reinvestigation of the case in the home by the local emergency relief administration.

(*c*) *Chronic illness.*—Medical care for prolonged illnesses, such as chronic asthma, chronic heart disease, chronic rheumatism, diabetes, etc., shall be authorized on an individual basis, and, in general, visits shall be limited in frequency (i.e., not more than 1 visit per week for a period not exceeding 2 or 3 months) by agreement. Nursing care for such chronic illnesses shall, in general, be authorized in accordance with the need for such care as indicated by the attending physician. If necessary, more frequent visits, by the physician or nurse, for an acute attack occurring in the course of a chronic illness, may be authorized. Care for chronic illness authorized under this section shall supplement and not supersede existing community services, such as visiting nursing service or institutional care.

(*d*) *Obstetrical care.*—Authorization for obstetrical service in the home shall include an agreed minimum number of prenatal visits (where possible), delivery in the home, and necessary postnatal care. Due caution shall be exercised that this authorization for delivery in the home does not involve undue risk to the patient for whom hospital care may be imperative. The physician authorized to attend the confinement in the home shall be responsible for certifying to the local relief administration that, in his professional judgment, delivery in the home will be safe.

(*e*) *Special services.* — Medical and nursing services not covered above shall be authorized on an individual basis, subject to the general provisions of the agreement made under regulation 1. Special dental service shall be subject to a similar procedure.

Medical care shall not ordinarily be authorized by relief administrations for conditions that do not cause acute suffering, interfere with earning capacity, endanger life, or threaten some permanent new handicap that is preventable when medical care is sought.

(*f*) *Accessory services.*—Emergency dental care and bedside nursing service, for indigent persons in their homes, may be authorized subject to the existing general policy of the State and/or local relief administration.

(1) *Dental care* shall, in general, be restricted to emergency extractions and repairs. Dentists and dental care shall be subject to the same general restrictions indicated for physicians under regulation 1.

(2) *Bedside nursing care,* where authorized, shall conform to a procedure comparable to the one outlined for physicians above, and shall be provided under an agreement made between relief administrations and nursing organizations, State and/or local, under the same principles suggested for physicians under regulation 1. Standards of accredited local nursing organizations shall be followed by nurses giving authorized bedside nursing care to indigent persons in their homes. Such authorized bedside nursing care shall not supersede or supplant existing local official services giving such care under the provisions of local law.

(*g*) *Fee schedules.*—The agreement between the State and/or local relief administration and the organized professional groups of physicians, nurses, and dentists, State and/or local, established under regulation 1, shall include a fee schedule covering the basic and special services outlined in sections (*b*) to (*f*), inclusive, of this regulation. In the interests of simplified accounting it is suggested: That a flat rate be established, on a per visit basis for the usual care given to acute and chronic illness (sections (*b*) and (*c*) above), for attendance at confinement (section (*d*) above), for emergency extractions (section (*f*) above), and for a bedside nursing visit (section (*f*) above); and that all special services (medical, nursing, or dental) be covered by an agreed reduction from the usual minimum fee schedule for such services with an agreed maximum fee. A recognized differential in fee shall be established between a home and an office visit. All fees shall be established on the basis of an appreciable reduction from the prevailing minimum charges for similar services in the State and local communities, with due recognition of the certainty, simplicity and promptness of payment that authorization from the local relief administration insures.

This schedule shall only apply where the expenditure of Federal Relief Funds is involved and shall not preclude the payment of additional amounts from local funds.

Where bedside nursing care is authorized, the flat rate per visit shall be established by agreement at not to exceed the certified cost per visit established for accredited visiting nursing organizations in the State or local district.

(*h*) *Bills.*—Physicians, nurses (or nursing organizations), and dentists who are providing authorized medical care to indigent persons in their

homes shall submit to the local relief official, monthly (within 10 days after the last day of the calendar month in which such medical care was provided), an itemized bill for each patient. Each bill shall be chronologically arranged and shall contain at least enough information to permit proper audit (i.e., name, age, and address of patient; general nature of illness or diagnosis; whether home or office treatment; dates of service; and status of case at end of month—cured, sent to hospital, dead, needs further care, etc.). Bills for medical care shall be accompanied by the original written order for such care, except for cases in which medical service under an authorization has not terminated during the calendar month covered by the bill, in which cases the bill shall show, in addition to the details required above, the date and serial number of the outstanding order. Retroactive authorizations shall not be issued or honored for payment.

Bills for special and accessory services, outlined under sections (*e*) and (*f*) above, shall give full details of such services, and bills for medicines and medical supplies, under (*i*) below, shall be subject to the same general requirements. Bills for drugs shall list the name and quantity of each. The formula and number of each prescription costing more than 25 cents shall be submitted with or made a part of the pharmacist's bill.

> NOTE.—The submission of bills and their audit and authorization for payment will be simplified if the State Emergency Relief Administration provides a suitable bill form.

(*i*) *Medicine and medical supplies.*—Physicians providing authorized medical care to indigent persons shall use a formulary which excludes expensive drugs where less expensive drugs can be used with the same therapeutic effect. When expensive medication is considered essential by the authorized attending physician it may be authorized after consultation with the local medical advisory committee.

Prescriptions for necessary drugs and medicine shall be restricted to the National Formulary or the United States Pharmacopeia. To avoid excessive expenditures for remedies of unknown or doubtful value proprietary or patent medicines shall not be authorized.

State and/or local relief officials are urged to make trade agreements with pharmaceutical organizations and druggists for uniform or reduced rates for prescriptions.

Authorizations for medical supplies shall be restricted to the simplest *emergency* needs of the patient consistent with good medical care.

In general, authorizations for medicine and medical supplies shall not be issued except upon written request of the physician authorized to attend the person for whose use they are desired.

3. *Authority.* — The State emergency relief administration, responsible for the distribution of Federal and State Emergency Relief Funds to local relief administrations, shall give approval to such statements of policy, proposed fee schedules, and detailed procedures, governing the provision of medical, nursing, and dental care in the home to recipients of unemployment relief, as may be established by State and/or local relief administrations, in accordance with the provisions of regulations 1 and 2, above, before such policies, schedules, and procedures shall take effect. It shall be the responsibility of the State emergency relief administration to formulate a program of medical, nursing, and dental care for indigent persons in their homes, which shall not be in conflict with the provisions of regulations 1 and 2, above, and to make sure, by giving or withholding approval, that analogous programs formulated by local relief administrations shall not be in conflict with such State program.

(*a*) *State and local professional advisory committees.* — State and local relief administrations shall request the presidents of the State and local medical, nursing, dental, and pharmaceutical organizations, respectively, to designate an existing committee or appoint a special committee to advise them in the formulation and adoption of adequate programs for medical, nursing, and dental care in the home for indigent persons. The relief administrations shall be responsible for the final adoption of such programs. The medical, nursing, dental, and pharmaceutical advisory committees can assist these administrations in maintaining proper professional standards and in enlisting the coöperation of the constituent, professional membership in such programs. Local medical, nursing, and dental programs submitted to the State relief administration for approval should be submitted to the appropriate professional advisory committee for comment, before final approval is given. The appropriate professional advisory committees should be consulted by relief administrations with regard to disputed problems of medical, nursing, and dental policy and practice.

(*b*) *Licensed practitioners of medicine and related professions.* — When a program of medical care in the home for indigent persons has been officially adopted, participation shall be open to all physicians licensed to practice medicine in the State, subject to local statutory limitations and the general policy outlined in regulation 1, above. Physicians authorized by relief officials to give medical care under this program shall have accepted, or shall be willing to accept, the regulations and restrictions inherent in such a program. In order to provide adequate medical care it may be desirable for local relief officials to maintain on a district basis a list or file of physicians in the community who have agreed in writing to comply with the officially adopted program. Such a list of physicians should also facilitate a more equitable distribution of orders for medical services.

A similar policy and procedure shall be followed in the preparation of approved lists of nurses, den-

tists, and pharmacists. Licensure and/or registration to practice their respective professions in the State shall be a prerequisite to approval of graduate nurses, dentists, and pharmacists for authorized participation in the officially approved State program for the provision of medical care for indigent persons in their homes.

(*c*) *State program for medical care to indigent persons in their homes.* — When the State emergency relief administration has adopted a uniform program for medical, nursing, and dental care for indigent persons in their homes, in accordance with these rules, a copy of such program, including the statement of policy, fee schedules, and detailed procedures, shall be filed immediately with the Federal Emergency Relief Administration.

A SORBONNE DEGREE FOR DR. HARVEY CUSHING

Announcement has been made that Dr. Harvey Cushing was awarded the insignia of Doctor Honoris Causa by the Sorbonne University at its opening session November 4, 1933.

President Albert LeBrun presided over the meeting, and Dr. Gustave Roussy, Dean of the Medical Faculty, paid tribute to the accomplishments of Dr. Cushing.

Dr. Cushing now occupies the John Sterling Chair of Neurology in the Yale University Medical School. He has been awarded many prizes and honorable mention by scientific organizations.

DR. LOUIS E. PHANEUF ADDRESSES THE BROOKLYN GYNECOLOGICAL CLUB

Dr. Louis E. Phaneuf addressed the Brooklyn Gynecological Club on Friday evening, November 3, the subject of his address being The Management of Uterine Prolapse.

THE APPOINTMENT OF DR. EDWARD W. WHITNEY

Dr. Edward William Whitney has been advanced from the position of assistant physician at the Northampton State Hospital to that of Superintendent of that institution, to succeed Dr. Theodore A. Hoch.

Dr. Whitney was a native of Putnam, Connecticut. He is a graduate of the Harvard Medical School, and was an intern at the Boston City Hospital. He is a member of the Massachusetts Medical Society.

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR OCTOBER, 1933

Whooping cough reached its highest October figure for eight years.

Anterior poliomyelitis is approaching its normal base line with a marked decrease over the preceding month.

Diphtheria and typhoid fever maintained their lowest incidence for this State.

For the first time since 1919, more than 1,000 cases of gonorrhea and syphilis have been reported for three months in succession.

Tuberculosis, pulmonary and other forms, continue their usual downward trend.

Lobar pneumonia, mumps, measles, German measles, scarlet fever, epidemic cerebrospinal meningitis, and chicken pox show nothing remarkable.

The incidence of dog bites remains high.

RARE DISEASES

Anterior poliomyelitis was reported from Arlington, 1; Boston, 5; Braintree, 1; Fall River, 1; Lawrence, 1; Lexington, 1; Medford, 1; Milton, 1; Montague, 1; Salem, 1; Somerville, 1; Taunton, 1; Weymouth, 1; Worcester, 6; Total, 23.

Dysentery was reported from Auburn, 1; Weymouth, 1; Total, 2.

Encephalitis lethargica was reported from Attleboro, 1; Chelsea, 1; Grafton, 1; Lynn, 1; Total, 4.

Epidemic cerebrospinal meningitis was reported from Boston, 1; Leominster, 1; Total, 2.

Malaria was reported from Attleboro, 1; Scituate, 1; Taunton, 2; Total, 4.

Septic sore throat was reported from Boston, 3; Danvers, 1; Everett, 1; Total, 5.

Tetanus was reported from Waltham, 1.

Trachoma was reported from Boston, 1; Stow, 1; Total, 2.

Trichinosis was reported from Arlington, 1; Brookline, 1; Holyoke, 1; Newton, 4; Total, 7.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

MONTHLY REPORT FOR OCTOBER, 1933

Disease	Oct. 1933	Oct. 1932	Average*
Anterior Poliomyelitis	23	4	98
Chicken Pox	280	344	392
Diphtheria	108	111	290
Dog Bite	459	387	405
Epidemic Cerebrospinal Meningitis	2	7	8
German Measles	12	27	29
Gonorrhea	671	579	547
Lobar Pneumonia	201	186	225
Measles	259	198	360
Mumps	163	216	196
Scarlet Fever	513	730	601
Syphilis	367	366	274
Tuberculosis, Pulmonary	258	307	359
Tuberculosis, Other Forms	39	38	43
Typhoid Fever	20	31	35
Whooping Cough	671	271	339

*Average number of cases for October during the preceding five years.

RECENT DEATHS

RICHARDSON—Frank Linden Richardson, M.D., of Newtonville, Mass., died while driving his automobile November 16, 1933. He was born in Concord, Mass., in 1877, the son of a pharmacist who conducted business in Cambridge. After attending schools in Concord he graduated from Massachusetts Institute of Technology and then entered the Harvard Medical School graduating in 1903.

He served an internship in the surgical department of the Boston City Hospital and subsequently became head of the anesthesia service in that institution, holding this position up to the time of his death. He was a consultant in anesthesia at the Children's Hospital and Beth Israel Hospital and lectured on this specialty at the Tufts College Medical School. He completed a motion picture on the use of anesthetics. He is survived by his widow, Mrs. Constance Mathey Richardson, and two sons, Paul H. Richardson and David A. Richardson; both are now students at the Massachusetts Institute of Technology.

He joined the Massachusetts Medical Society in 1904 and was a member of the Boston Society of Anesthetics, the International Anesthesia Research Society and the Harvard Club of Boston.

WEST—George Leon West, M.D., of Newton Center, died at the Newton Hospital, November 18, 1933, of an acute heart attack. He was born in Biddeford, Maine, in 1868, the son of George S. West and Mary R. (Lapham) West. His early education was acquired in the place of his birth and the Boston Latin School. He received his A.B. degree from Harvard College and his M.D. degree from the Harvard Medical School in 1894. He was also awarded the A.M. degree. He served as house officer at the Boston City Hospital and began practice in Newton in 1895. Since 1897 he had been a member of the staff of the Newton Hospital, first as pathologist and later on the Executive Staff. He was also a trustee and medical director of the same hospital. He was a member of the Newton board of health and the board of public safety. During the World War he was a member of the draft board. His associates felt that his strenuous labor on government work was the cause of impaired health. He was medical examiner of his district and was reappointed for another seven-year term a week before his death. He was past president of the Massachusetts Medico-Legal Society, the Newton Medical Club, the Medical Examiners' Association and the Middlesex South District Medical Society. He joined the Massachusetts Medical Society in 1894.

Dr. West married Mabel Worthing Merrill in 1891. He is survived by a daughter, Mrs. Alice Mara Craig, wife of Dr. George M. Craig, of Middletown, Conn.; a son, Worthing Lapham West of Newton Centre; two sisters, Mrs. Ethel Gutridge of Kingston, N. Y., and Miss Mary L. West of Newton; also a brother, Winfield C. West of Newtonville.

RICHARDS—George Lyman Richards, M.D., died November 9, 1933, at South Yarmouth, Massachusetts. He was born in Farmington, Connecticut, June 1, 1863, the son of Solomon and Myra E. (Lyman) Richards. He was a graduate of the Williston Seminary, Easthampton, and received his M.D. degree from the Harvard University Medical School in 1886. He subsequently studied in Europe at the Universities of Vienna, Halle, Strassburg, and Freiburg, and at universities in England. Previous to settling in Fall River in 1895, he had served at the Rhode Island Hospital, Howard, R. I., East Greenwich, R. I., and Marion, Mass. At various times he engaged in work in France, Germany, China, Turkey and India. He had retired from active practice.

He was formerly a member of the staffs of the Union and City Hospitals of Fall River and the Cape Cod Hospital in Hyannis. He also conducted a clinic in New Bedford. His standing in otolaryngology gave him membership in important organizations in the United States, among which were the Massachusetts Medical Society, the Massachusetts Board of Registration in Medicine, American College of Surgeons, the American Otological Society, the American Laryngological Association, the American Medical Association, the American Laryngological, Rhinological and Otological Association, the American College of Surgeons, and numerous others.

He married Mary L. Robinson of Boston, who was killed in an automobile accident in 1927. He is survived by his widow Christine M. (McLean) Richards, and a son, Dr. Lyman Richards, of Boston.

At a meeting of the Fall River Medical Society last September, Dr. Richards was presented with a silver platter as a testimonial to his outstanding qualities. He was a Mason, a member of the Harvard, University and Congregational Clubs. He had contributed many scientific articles to medical journals, and was the author of the book entitled "Nose and Throat for the General Practitioner."

SCHNEIDER—Jacob Philip Schneider of 12 Pleasant Street, Palmer, Massachusetts, died at his home November 12, 1933. He was born in Greenfield, Massachusetts, April 19, 1867, the son of William and Margaret Schneider. His early life was spent in Orange and Westfield. He studied medicine under Dr. Gamwell of Westfield, and graduated in medicine from the University of Vermont Medical School in 1894, afterward serving as house physician of the Springfield Hospital.

Dr. Schneider moved to Palmer two years later, was medical examiner for 25 years, and a surgeon to the Boston and Albany railroad. He was a member of the draft board during the World War, and had served the town as chairman of the Palmer Board of Health for many years.

He joined the Massachusetts Medical Society in 1898. His religious affiliations were with the Congregational Church. He is survived by his widow, Mrs. Margaret Schneider, one son, Philip, one

daughter, Margaret, and a brother, Dr. Harry Schneider of Michigan.

HORSMAN—Hiram L. Horsman, M.D., died at North Grafton, November 13, 1933, following a short illness. He was assistant superintendent of the Grafton State Hospital. He was born in Princeton, Maine, in 1870, and graduated from Bowdoin College in 1893, and from the Bowdoin Medical School in 1899. He served at the Summer Street Hospital, and at the North Grafton State Hospital for the past twenty-one years. He was a Mason, and a Fellow of the Massachusetts Medical Society having joined in 1914.

Besides his widow, he leaves two sons, Lionel, a student at Bowdoin College, and Donald, a student at Hebron Academy.

OBITUARY

EDGAR DWIGHT HILL

1854-1933

A Personal Tribute

"He was a man, take him for all in all,
I shall not look upon his like again."

Our kind loving and dear friend is dead. No more with his hearty handshake, his genial smile, his keen wit will he greet us. We knew him intimately in the vigor of his manhood and his mature years. His disposition was always the same; generous, charitable, a prince of good fellows; no social gathering was complete without his presence. He numbered his friends by the legion. He possessed that indescribable quality called personal magnetism, to a marked degree. Few men have it; it cannot be acquired; wealth cannot purchase or influence procure it. It is that mysterious characteristic which attracts men and holds them in loving friendship. It is inherent in one's nature.

For fifty-five years he actively practiced his profession, and did not relinquish his work until death took him from us. A keen diagnostician exercising his common sense, using the faculties with which his Creator endowed him to a marked degree. Ready in all emergencies, he was admired for his professional ability.

In my imagination I can picture him in the early years of his career. Saturated with ambition for success in the vocation he had chosen for his lifework, full of energy, he is able and willing to work. In the torrid heat of summer, in the frigid cold and storms of winter, no call too far, no weather too severe, no road too rough, night or day he responds to the call of rich and poor alike. His faithful horse clattering over the steep and rocky slopes and his ancient buggy are his conveyance. The women folk smile as he drives by and he waves his hand in friendly greeting. Little children shout, "My Doctor." He reaches the old farmhouse nestled among the hills and spends the night or many weary hours at the bedside of a retarded maternity case.

He has become more than a physician to these people; he is their friend and counsellor to whom they pour out all their troubles, both mental and physical. He is their father confessor to whom they apply in times of distress and affliction and at the hour of death and sadness consoles them as no other can.

Alas! the old country doctor is fast disappearing, his place is now filled by the man of science who diagnoses their ailments with instruments of precision; the intimate contact is lacking, that implicit confidence is gone. The modern physician well remembers he has a fee to receive and sometimes forgets he has a duty to perform.

No physician practicing in the historic Town of Plymouth influenced by the events of the past, actuated by the example of those noble pioneers of the past, could fail. The life of our friend was a success; though not endowed greatly with the material goods of this world, his influence on the community in which he served and the esteem in which he was held constitute the criterion. Does it follow because his name was not proclaimed in the press or from the rostrum he was not doing the duty which the Almighty assigned to him?

No wonderful discoveries in medicine or surgery heralded his name. No sensational events in his life are recorded, he pursued the even tenor of his way, the country doctor beloved by all. His name will be revered and remembered long after the temporary fame of others has faded from our minds.

There were many brighter lights; there may have been scintillating stars which adorned with their brilliancy the firmament of the medical profession, but none were held in more endearing love and esteem than the humble physician of whom I speak. When his spirit passed away to that bourne from whence no traveler returneth, a niche, hard to fill, was vacant in the sphere he occupied.

May God in His infinite mercy grant unto him eternal rest.

Thomas H. McCarthy, M.D.

Brockton, November 14, 1933.

NOTICES

The Massachusetts Medical Society

ESSEX SOUTH DISTRICT

Postgraduate Medical Course

A series of ten exercises has been arranged at the Auditorium of the Nurses' Home of the Salem Hospital on Tuesdays from 4 to 6 P. M. The first was given on November 14, 1933. The schedule, which is subject to change, follows:

November 28—Gastro-Intestinal Diseases.
December 5—Gastro-Intestinal Diseases.
December 12—Acute Infections.
December 19—Diseases of Blood.
December 26—Medical and Surgical Emergencies.
January 2—Endocrinology.
January 9—Arthritis.
January 16—Diabetes and Vitamins.

Registration fee of $5 must be paid at the first exercise attended.

WALTER G. PHIPPEN, *District Chairman.*

A CLINIC FOR PATIENTS WITH MIGRAINE

A special clinic for the study and treatment of patients having periodic headaches (typical or suggestive of migraine) is being held at the Out-Patient Department of the Boston City Hospital. This clinic meets on Monday afternoons at two o'clock in the Neurological Department. Patients who are residents of Boston will be seen in this clinic without charge. For the present, previous appointment is not necessary. If the referring physician wishes a report of findings, he should send a note to this effect with the patient.

STANLEY COBB, M.D.

A CORRECTION

The printer failed to follow the corrected text of President Lowell's address in the Sesquicentennial Celebration of the Harvard Medical School. The garbled sentence as printed is as follows: "The object of a medical school is not to train practitioners but to train investigators also." It should have read "The object of a medical school is not only to train practitioners but to train investigators also."

This was a most unfortunate error for which the editorial staff was not responsible.

MASSACHUSETTS GENERAL HOSPITAL

The exercises at the Massachusetts General Hospital on Thursday forenoons are of especial interest to physicians. For details see the regular announcement on page vi.

REPORTS AND NOTICES OF MEETINGS

THE MASSACHUSETTS MEDICAL BENEVOLENT SOCIETY

The Annual Meeting of the Massachusetts Medical Benevolent Society was held at the Boston Medical Library on Thursday, October 26, 1933. Dr. Roger I. Lee, the Treasurer, reported that at present there were twenty-three beneficiaries, either doctors who need help because of old age or illness, or their families. During the past year, two of these were added to the list and one of last year's beneficiaries had died and, therefore, had been dropped from his list. He spoke of the excellent result which had been obtained through a vote of the Society last year which allowed the Society to accept and disburse on the checks of the Society to individuals generally, irrespective of whether they were beneficiaries. This vote was intended to permit generous individuals to give sums of money to worthy people and yet maintain the anonymity of donors and relieve the recipients from possible embarrassment.

The gift in the will of Dr. George W. Gay to the Society of $1000 was again commented on.

The Society elected as officers the following:

President: Dr. George Gray Sears.

Vice-President: Dr. Robert Montraville Green.

Secretary: Dr. Hilbert F. Day.

Treasurer: Dr. Roger I. Lee.

Trustees for Three Years: Dr. Lincoln Davis, Dr. George S. C. Badger, Dr. William B. Robbins.

The following remarks by Dr. Robert M. Green about our former Treasurer, Dr. William Lambert Richardson were read and appreciated:

The death of Dr. William L. Richardson has removed from our professional life a distinguished figure, active until quite recently, belonging to a much older medical generation than our own, a generation which included among others such names as Buckingham, the elder Cheever and Fitz, Gay, the two Shattucks, Walcott, Warren and Wyman. At the time of his death Dr. Richardson was second in academic seniority among the Emeritus Professors of Harvard University, a position to which Dr. Abner Post now succeeds.

William Lambert Richardson was born on September 6, 1842, at the home of his parents, which was on the corner of Pearl and High Streets in Boston. His father, Jeffrey Richardson, was a prosperous merchant and his mother, who before her marriage was Julia Lambert Brackett, belonged to a well-known Boston family. Their home at that time was in the residential district which then extended near to the commercial regions of the waterfront. After his early schooling, young Richardson entered Harvard College in 1860, graduating with the degree of A.B. in 1864. He was elected Secretary of his class and served in this office for sixty-eight years. From College he passed directly to the Harvard Medical School from which he graduated with the degrees of A.M. and M.D. in 1867. Immediately thereafter he went abroad to complete his medical studies which he pursued in Vienna and at the Rotunda Hospital in Dublin bringing back from these two cities the latest of progress in German and Irish obstetrics.

Beginning the practice of Medicine in Boston in 1868, Dr. Richardson was at first appointed to the Staffs of the Massachusetts General Hospital, the Children's Hospital, and the Boston Dispensary. He was one of the first to specialize in obstetrics, and in 1873 he resuscitated the old Boston Lying-in Hospital, then located in a single brick building on McLean Street. In 1875 he became Secretary of the State Board of Health and served in this capacity for several years. In 1871 he was appointed Instructor in Obstetrics at the Harvard Medical School, became Assistant Professor in 1882, and Professor of Obstetrics in 1886.

Among Dr. Richardson's manifold activities was his association with the Boston Lying-In Hospital which constituted his outstanding life work and it it with this institution that his memory is chiefly identified. He worked unceasingly at the Hospital

and for its interests. The building on McLean Street was progressively enlarged and remodeled under his fostering care. In 1888 its Training School for Nurses was established. Finally in 1922 the Hospital was removed to its new building on Longwood Avenue, opposite the Harvard Medical School, and at this time, after fifty years of service, Dr. Richardson became President Emeritus of its Board of Overseers. During this half century of his active connection with the Hospital, 75,000 patients were delivered under its care and 291 physicians obtained their training as its obstetric house officers. It was Dr. Richardson's ambition to make this Institution not only a place of service to the community but one of the great obstetric hospitals of the world, and in this he succeeded as he did in virtually everything he undertook. As a result of his devotion and that of his associates, the Boston Lying-In Hospital ranks today with such institutions as the Dublin Rotunda, Queen Charlotte's Hospital in London, and the Sloane Maternity of New York.

Throughout his long connection with the Lying-In Hospital, Dr. Richardson carried on the teaching of obstetrics in its wards and in the Harvard Medical School. In addition to his professorial duties, he served as Dean of the Medical School from 1893-1907, and as Dean of the Faculty of Medicine from 1899-1907. Upon his retirement from active teaching in the latter year, he was made Professor of Obstetrics Emeritus. From 1909-1915 he served on the Board of Overseers of Harvard College and in 1926 received the honorary degree of S.D. from this University.

As one of the collateral activities of his life, Dr. Richardson was extremely interested in military affairs and for thirty-five years, from 1870 to 1905, served as Surgeon of the First Corps of Cadets, Massachusetts Volunteer Militia. He was a member of many medical and scientific societies including the American Academy of Arts and Sciences, the American Gynecological Society, the American Public Health Association, the Massachusetts Medical Society and the Massachusetts Medical Benevolent Society. For thirty years Dr. Richardson was Treasurer of the Massachusetts Medical Benevolent Society and it was chiefly due to his sagacious administration of its funds that the Society has been able to render its extensive assistance to destitute physicians and their dependents.

On July 25, 1867, Dr. Richardson was married in Portland, Maine, to Miss Olivia L. Aitchison Pillsbury who died in 1887. There were no surviving children and for the remainder of his life Dr. Richardson's existence was solitary, save for the many contacts of his professional and public activities.

To all of us who knew him, Dr. Richardson's intense, vigorous, and unusual personality is so familiar that it needs no description. Swift and accurate in observation and judgment, his sagacity was unerring. A man of few and abrupt words, he seemed to some brusque and austere; but those who knew him came to appreciate the warm current of underlying kindlinesses which ran through his whole life. The majority of his acts of helpfulness and benefaction to others are unrecorded but none the less genuine and sincere.

After a life time thus filled with constructive activity and service, Dr. Richardson withdrew at the close to the seclusion of his home and the companionship of a few old and intimate friends; and thus with relatively little physical disability at the end he died quite suddenly and without suffering on October 20, 1932, in the ninety-first year of his age. At his funeral services held on October 24 at the Arlington Street Church, of which he was a life-long member, the Rev. Samuel A. Eliot said of him:

"Here was incarnated the common sense, the public spirit, the humorous way of looking at things, the clear integrity, the practical idealism of our New England heritage. By that compulsion of nature which is a call of God he undertook the laborious career of a physician and found deep satisfactions in the ministry of healing. His energies ever widened with increasing responsibilities and he became not only the beloved and trusted doctor, but also the wise and efficient administrator of great trusts, the guide and pioneer of medical education, the founder of institutions for the comfort of those in distress of body and in peril of pain and death. He walked worthy of the vocation to which he had been called, caring for the sick in their necessity, speaking the truth in sincerity and good will, ingeniously directing research and crowning his wisdom with the essential grace of common sense.

"Humanity meant to him more than its differences, and his influence and intercourse with all sorts and conditions of men levelled up and raised the grade of all of us who came in contact with him. He fought disease, relieved pain, turned anxiety into joy. We caught the contagion of his pluck and patience. He rang true in every relation of life. He was upright and downright, sane and sure. It was a life abundant in friendship but dependent neither on praise nor blame. To accept the day's duties and pleasures with resolute goodwill and an abundant delight in every opportunity of service—that was his privilege and part. The confidence and affection of a grateful community attended him in life and death."

In another context, Dr. William D. Sohier, one of Dr. Richardson's life-long associates and friends, wrote similarly:

"Invariably cheerful, hopeful, courageous, he radiated hope and comfort in every ward or sick room he entered, inspired the nurses and the family. The patient, too, felt greatly encouraged by his visit, his manner and cheerful voice. He made the best possible of his gravest situations. He breathed hope, never say die, never gave up till the heart ceased to beat.

"To us who knew him, served with him and under him, the greatest achievement of his life was the sense of duty, the value of high courage and as-

pirations, the never-give-up attitude that radiated from his virile, electrical, magnetic personality."

From appreciations such as these, from our own recollections of him, from the many excellent things which he did, Dr. Richardson's personality and memory will long outlive us all in the community which he so abundantly served.

HILBERT F. DAY, M.D., *Secretary.*

HARVARD MEDICAL SOCIETY

The Harvard Medical Society met in the amphitheatre of the Peter Bent Brigham Hospital on Tuesday evening, October twenty-fourth. Dr. David L. Edsall presided.

A surgical and a medical case were first presented. The first patient was a forty-eight year old man whose chief complaints were right-sided headache of three months' duration, and blurred visión of fourteen days' duration. Early in the summer the patient had been suddenly seized with right temporal pain. The pain persisted, and at times was throbbing in character and very sharp. The patient became increasingly tired, and on one occasion became disoriented for a short time. Later his speech became inarticulate during a telephone conversation. One month before entry he had five minutes of pain and numbness in his left leg, and two weeks before entry he complained of blurred vision, went to an oculist, and was referred to the Brigham Hospital. There were several noteworthy findings on physical examination. There was an exostosis over the right temporal region. There was a diminished nasolabial fold on the right. There were five diopters of choking of the optic disc on the right, and four to five on the left. Ventriculograms showed an extensive flat tumor in the frontal region of the brain. A right parietofrontal bone flap was done and an encapsulated subdural hematoma removed. Convalescence was proceeding satisfactorily.

The second patient was a middle-aged man who complained, on entry, of a dry hacking cough of three years' duration and pain in the knees and legs for the past six months. For three months the patient had coughed up considerable viscid, yellow sputum. For eight weeks he had had considerable generalized bone and joint pain. During the previous year he had lost twenty-five pounds in weight. On examination the patient was moderately dyspneic and cyanotic, and coughed considerably. Emphysema and arteriosclerosis were in evidence. There was an area of flatness with absent breath sounds in the right chest, and an area of dullness with diminished breath sounds over it. Coarse rhonchi were readily heard. The forearms and knee joints were swollen. There was marked tenderness over the long bones, and clubbing of the fingers. On admission the hemoglobin content of the blood was 70 per cent, the red blood cell count 3,650,000, and the white count 12,000. The urine was negative. The sputum contained many organisms, fungi belonging to the monilia group, x-ray films of the chest showed partial consolidation and atelectasis of the right lung, as well as a process thought to be a chronic pneumonitis. The long bones showed a localized, symmetrical periostitis, the picture of chronic pulmonary osteoarthropathy. The patient has been treated with inhalations of ethyl iodide, and intravenous arsphenamine. In discussing the case Dr. Christian pointed out how this disease might be confused with arthritis and tuberculosis and pointed out the differential features of each. Dr. Fitz mentioned the work he had recently seen in the South on the use of vaccines as well as iodides in treatment.

The main addresses of the evening were on "Experiences with High Temperatures at Boulder City, Nevada, with Some Clinical Applications," by Drs. D. B. Dill, and Arlie V. Bock. Dr. Dill told mainly of the experimental work done in Nevada by the expedition of which the speakers were members on the composition of the sweat produced by the working men. In the normal man subjected to such high temperatures (120-150) degrees Fahrenheit there are no obvious changes in the properties of the blood. The sweat varies much, though, in quantity and quality. The constituents and amount of sweat secreted under various conditions were estimated fairly accurately by determining the differences between normal urine and the urine of the working man, as well as by making actual analyses of the sweat. The fluid intake, of course, was kept constant. It was found that the salt content of sweat varies between a tenth and an eighth of that in the blood serum. A man working in an environment of such high temperatures lost considerable body salt during his work. Weight loss and so-called "heat cramps" followed if the salt was not replaced; that is, water alone was not enough.

Dr. Bock went on to talk more specifically of heatstroke. Three theories, in general, have been advanced to explain "heat cramp": (1) that it is due to an acute degenerative process in the muscles (Edsall), (2) that toxic substances from the overgrowth of tetanus bacilli in the gastro-intestinal system are liberated, and (3) that it is due to lack of sodium chloride. The workers at Boulder City were able to produce immediate relief from the cramps by the parenteral administration of one to two liters of isotonic sodium chloride. The speaker next discussed the effects on the body of prevention of the radiation of body heat. There is generalized fatigue and a more or less rapid pulse rise. The chief contributory cause in heat death seems to be circulatory failure. Heat deaths are thus prevented by an understanding of the necessity for and therapeutic use of sodium chloride, and elimination of the circulatory unfit. Dr. Bock concluded with a discussion of the use of sodium chloride in everyday medical practice. From the experimental side, evidence of the value of salt is readily obtained. Dogs with complete jejunal obstruction died in about 108 hours unless salt was administered, when they lived for 31 days. "Water intoxication" is prevented by the use of some salt. Sodium chloride must be used to combat dehydration in pneumonia, other acute infections, and diabetic coma. It is Dr. Bock's opinion that patients with pneumonia do better clinically when they are given sodium chloride. The

substance is also an adjunct in the treatment of coronary thrombosis.

In closing the brief discussion at the end of the meeting Dr. Edsall mentioned the two things necessary for the production of "heat cramps," very high temperature and very hard muscular work. Individuals vary much in susceptibility. The enormous nitrogen, phosphorus, and sulphur breakdown in the disease make Dr. Edsall feel that lack of sodium chloride is not the whole story.

BOSTON CITY HOSPITAL

STAFF CLINICAL MEETING

Wednesday, December 13, 1933, at 8:15 P.M.
Thorndike Amphitheatre

Nephrectomy in Renal Tuberculosis and the Value of Long-Continued After Care. Dr. Herbert H. Howard. (Discussion by Dr. George Gilbert Smith.)

Nephropexy for Ureteral Kinks. A Review and Results of Ninety Cases. Dr. Augustus Riley. (Discussion by Dr. J. Dellinger Barney.)

Perineal Injection of Mercurochrome in Prostatic and Vesicular Infections. Dr. Gordon D. Atkinson.

Treatment of Acute Gonorrheal Arthritis of Knee. Dr. William F. Cotting. (Discussion by Drs. H. H. Howard, A. Riley and O. J. Hermann.)

COMMITTEE ON HOSPITAL CLINICS.

NEW ENGLAND DERMATOLOGICAL SOCIETY

The next meeting of the New England Dermatological Society will be held on Wednesday, December 13, at 3 P.M., at the Boston City Hospital.

J. HARPER BLAISDELL, *Secretary.*

THE NORFOLK DISTRICT MEDICAL SOCIETY

A regular meeting of the Society will be held in the Roxbury Masonic Temple, 171 Warren Street, Roxbury, November 28, 1933, at 8:15 P.M. Telephone GAR 9492.

Business: Reports of Committees.

Communications: The Massachusetts Pneumonia Program. Dr. Roderick Heffron. The Diagnosis and Treatment of Lobar Pneumonia. Dr. Frederick T. Lord. Surgical Treatment of Empyema. Dr. Edward D. Churchill.

Collation.

FRANK S. CRUICKSHANK, M.D., *Secretary.*
1695 Beacon Street, Brookline.

SUFFOLK DISTRICT MEDICAL SOCIETY

POSTGRADUATE INSTRUCTION

The Suffolk District Medical Society Extension Course will begin on Wednesday, November 29, 1933.

Subject: "Vascular Disease."

Instructors: Dr. Herrman L. Blumgart and Dr. Louis Wolff.

Time and Place: 3:00-5:00 P.M. at the Beth Israel Hospital.

All Fellows of the Society who plan to take this course should report at the Beth Israel Hospital on the above date. At this meeting the time and place of future meetings will be decided. All members of Suffolk District are welcome to take this course, which will consist of a series of ten subjects as follows:

Vascular Disease
Practical Medical Principles for Everyday Use
Gastro-Intestinal Disease (A)
Gastro-Intestinal Disease (B)
Acute Infections
Diseases of the Blood and Hematopoietic System
Medical and Surgical Emergencies
Endocrinology
Vaccine Therapy
Arthritis.

The stated monthly meeting of the Suffolk District Medical Society will be held at the Beth Israel Hospital in the evening after this session.

At this stated meeting a new and interesting advancement in the treatment of cardiovascular disease will be presented. This should be of interest and benefit to those taking the Postgraduate Course. FRANK R. OBER, M.D., *Chairman.*

NOVEMBER MEETING

The November meeting of the Suffolk District Medical Society will be held on Wednesday, November 29, 1933, at 8:15 P.M., at the Beth Israel Hospital.

PROGRAM

1. Regional Ileitis—Dr. Charles G. Mixter.
2. Brill's Disease.
   a. Clinical Aspects—Dr. Harry Linenthal.
   b. Discussion—Dr. Hans Zinsser.
3. Complete Ablation of the Thyroid Gland in the Treatment of Angina Pectoris and Congestive Heart Failure.
   a. Medical Aspects — Dr. Herrman L. Blumgart.
   b. Surgical Aspects—Dr. David D. Berlin.

JAMES H. MEANS, M.D., *Vice-President,*
GEORGE P. REYNOLDS, M.D., *Secretary.*

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held in the Peter Bent Brigham Amphitheatre (Van Dyke Street entrance), Tuesday evening, November 28, at 8:15 o'clock.

PROGRAM

Presentation of Cases.

Functioning Malignant Tumors of Ductless Glands. By Dr. Shields Warren.

Multiple Primary Cancer. A Study of Cancer Susceptibility. By Dr. Charles C. Lund.

JOHN HOMANS, M.D., *Secretary.*

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

November 23—Massachusetts Society for Mental Hygiene will hold its annual meeting at the Twentieth Century Club, Boston, beginning with a luncheon at 1 o'clock.

November 23—Clinic at the Peter Bent Brigham Hospital Amphitheater, at 3:30 P.M.

November 24—The Edward K. Dunham Lecture will be delivered at the Harvard Medical School Amphitheater, Building C.

Genetics and Pathology

Friday, November 24 — "Intersexuality. X-rays and heredity. Alcohol and heredity. The tumor problem. Intermarriage and crossing. Some bearings of genetics on medical practice."

At five o'clock at the Harvard Medical School Amphitheater, Building C. By Otto Lous Mohr, M.D., Professor of Medicine, the Royal Frederiks University, Oslo.

November 27—New England Heart Association will meet in the Amphitheater of the Peter Bent Brigham Hospital at 8:15 P.M.

November 28—Harvard Medical Society. See page 1083.

December 7—Faulkner Hospital Clinical Meeting at 5 P.M. In addition to the usual pathological conference on the cases which have come to autopsy during the month Drs. F. J. Cotton and Henry C. Marble will talk on "Traumatic Surgery."

December 8 - May 11—William Harvey Society. For further information address Dr. Robert T. Phillips, Boston City Hospital, Boston.

December 13—New England Dermatological Society. See page 1083.

December 13—Boston City Hospital, Staff Clinical Meeting. See page 1083.

December 15 and 16—The American Board of Dermatology and Syphilology will hold oral examinations in New York City. Information may be obtained from the Secretary, Dr. C. Guy Lane, 416 Marlborough Street, Boston, Mass.

December 17, January 15—Boston Medical History Club.

Program:

December 17, 1933—Professor Norman E. Himes, of Colgate University, "Medical History of Contraception."

January 15, 1934—Professor Henry E. Sigerist, Director of the Institute of Medical History of Johns Hopkins University.

JAMES F. BALLARD, Secretary.

Boston Medical Library, 8 The Fenway, Boston.

February 16 and 17—The New England Hospital Association is holding its Twelfth Annual Meeting at the University Club, Boston. For details write Dr. A. G. Engelbach, Massachusetts General Hospital, Boston.

April 16-20, 1934—The American College of Physicians will hold its Eighteenth Annual Clinical Session in Chicago at the Palmer House. For information write Mr. E. R. Loveland, Executive Secretary, 133-135 South 36th Street, Philadelphia, Pa.

July 24-31, 1934—The IVth International Congress of Radiology will be held in Zurich under the presidency of Professor H. R. Schniz. General Secretary Dr. H. E. Walther, Gloriastrasse 14, Zurich.

September 4, 5, 6, 1934—International Union Against Tuberculosis will be held in Warsaw. For particulars address The National Tuberculosis Association, 450 Seventh Avenue, New York, N. Y.

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH DISTRICT MEDICAL SOCIETY

November 28 - January 16—Postgraduate Medical Course. See page 1079.

Wednesday, December 6—Beverly Hospital. Clinic 5 P.M. Dinner 7 P.M. Speaker: Dr. Henry Pollock, Superintendent of Massachusetts Memorial Hospitals. Subject: "Some Problems in the Administration of the General Hospital."

Wednesday, January 3—Danvers State Hospital. Clinic 5 P.M. Dinner 7 P.M. Speaker: Dr. Clarence A. Bonner, Superintendent of Danvers State Hospital. Subject: Recent Experiences in Foreign Clinics.

February 7—Council Meeting, Boston.

Wednesday, March 7—Lynn Hospital. Clinic 5 P.M. Dinner 7 P.M. Speaker: Dr. Frank H. Lahey, Boston. Subject to be announced. Film Electrocardiogram.

Wednesday, April 4—Essex Sanatorium, Middleton. Clinic 5 P.M. Dinner 7 P.M. Speakers: Dr. Elliott P. Joslin and Dr. Howard F. Root, Boston. Subject: "Tuberculosis Complicating Diabetes."

Thursday, May 3—Censors' Meeting, at Salem Hospital, 3:30 P.M.

Tuesday, May 8—Annual Meeting. Salem Country Club, Forrest Street, Peabody. Dinner at 7. Speaker to be announced. Subject to be announced.

RALPH E. STONE, M.D., Secretary.

221 Cabot Street, Beverly, Mass.

FRANKLIN DISTRICT MEDICAL SOCIETY

Meetings will be held on the second Tuesday of January, March and May at the Weldon Hotel, Greenfield, at 11 A.M

CHARLES MOLINE, M.D., Secretary.

Sunderland, Mass.

MIDDLESEX EAST DISTRICT MEDICAL SOCIETY

Meetings will take place on January 10 at Melrose; March (2nd Wednesday) at Wakefield, and May (2nd Wednesday) at Winchester.

ALLAN R. CUNNINGHAM, M.D., Secretary.

76 Church Street, Winchester, Mass.

MIDDLESEX NORTH DISTRICT MEDICAL SOCIETY

Meetings will be held on January 31, and April 25 (Annual Meeting).

T. A. STAMAS, M.D., Secretary.

226 Central Street, Lowell, Mass.

NORFOLK DISTRICT MEDICAL SOCIETY

November 24—Postgraduate Course.

November 28—Roxbury Masonic Temple, 8 P.M. See page 1083.

January 28—Tentatively Roxbury Masonic Temple, 8 P.M. Continuance of Symposium on Diseases of the Blood. Dr. Dameshek and Dr. Straus.

February 27—Place, time, subject, and speaker to be announced.

March 27—Place and time to be announced. Dr. Edward A. Edwards and Dr. Henry H. Faxon. Symposium on the Treatment of Varicose Veins.

May—Annual Meeting. Place, time and program to be announced.

FRANK S. CRUICKSHANK, M.D., Secretary.

1695 Beacon Street, Brookline, Mass.

NORFOLK SOUTH DISTRICT MEDICAL SOCIETY

December 7—12 noon at Quincy City Hospital. Program by the hospital staff.

January 4—12 noon at Norfolk County Hospital. Speaker to be announced.

February 1—12 noon at Norfolk County Hospital. Stated Meeting. Speaker: Dr. Sara Jordan. Subject: Stomach Ulcers.

March 1—12 noon at Quincy City Hospital. Program by the hospital staff.

April 5—12 noon at Norfolk County Hospital. Speaker: Dr. Elliott P. Joslin. Subject: Diabetes.

May 3—12 noon at Norfolk County Hospital. Annual Meeting. Election of Officers.

N. R. PILLSBURY, M.D., Secretary.

Norfolk County Hospital, South Braintree, Mass.

SUFFOLK DISTRICT MEDICAL SOCIETY

November 29—Postgraduate Instruction. See page 1083.

November 29—Clinical Program at the Beth Israel Hospital. See page 1083.

January 31—General Meeting in association with the Boston Medical Library and the Trudeau Society. Speaker: Dr. Lawrason Brown of Saranac Lake.

March 28—Clinical Meeting at the Massachusetts Memorial Hospitals.

April 25—Annual Meeting at the Boston Medical Library. Election of Officers. Scientific Program, titles and speakers to be announced.

The Medical Profession is cordially invited to attend all of these meetings.

JAMES H. MEANS, M.D., Vice-President.
GEORGE P. REYNOLDS, M.D., Secretary.
311 Beacon Street, Boston, Mass.
ALEXANDER S. BEGG, M.D.,
Boston Medical Library.

WORCESTER DISTRICT MEDICAL SOCIETY

All meetings to be held on Wednesdays as follows:

December 13—Dinner and scientific program at St. Vincent Hospital, Worcester, Mass.

January 10—Dinner and scientific program at the Worcester City Hospital, Worcester, Mass.

February 14—Dinner and scientific program at the Worcester State Hospital, Worcester, Mass.

March 14—Dinner and scientific program at the Memorial Hospital, Worcester, Mass.

April 11—Open date.

May 9—Annual Meeting. Time and place to be announced later.

ERWIN C. MILLER, M.D., Secretary.

27 Elm Street, Worcester, Mass.